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EXPERIMENTAL RENAL DISEASE PRODUCED BY X RAYS: PRODUCTION AND FUNCTIONAL STUDY OF A STANDARDIZED LESION.

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and

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The histological changes in the kidney following the application of measured doses of X rays under certain standardized conditions have been dealt with in a previous article.[1] The scope of the present article will be confined to the clinical course and functional changes during the progress of the lesion which follows this application.

Though much in demand, a standardized experimental nephritis has not yet been produced, although numerous attempts have been made and various techniques used. Before describing our own experiments we shall briefly mention the main lines of attack hitherto employed.

Toxic Nephritis.

Nephritis produced by means of substances having a toxic action on renal tissue has been observed by many workers, but lesions of sufficient chronicity for experimental study, when they are obtained, vary greatly and their constant production is uncertain. Moreover, these substances usually do not act specifically on the kidney, but have a deleterious action on other organs as well. Mercuric chloride, for instance, which is well known to be capable of producing nephritis, has other widespread effects, for instance it causes fatty degeneration of the liver, gastro-intestinal irritation and other lesions.

Operative Procedures.

Removal of Kidney Substance.

Renal insufficiency can be produced by removal of kidney substance until there is not sufficient left to maintain life. The technique of this procedure is difficult and, moreover, a true nephritis is not produced. Either sufficient hypertrophy of the remaining kidney tissue takes place for life to be maintained more or less as usual or there is not sufficient renal tissue left to maintain life. It is, however, possible to produce an experimental nephritis by functional overstrain on the diminished kidney tissue, as shown by Allen, Scharf and Lundin[2] and others, but production of a standardized lesion by this method would be in the face of considerable experimental difficulties.

Interference with the Blood Supply of the Kidney.

Interference with the blood supply of the kidney is open to similar objections. With ligation of branches of the renal artery atrophy or necrosis of the corresponding portion of the kidney will occur, followed by compensatory hypertrophy of the remaining portion or rapid death if the procedure has been too radical.

Production of Experimental Hydronephrosis.

With complete obstruction of the ureter by ligation, followed after a variable interval by uretero-cysto-neostomy (Hinman[3]), the kidney either returns completely to normal after relief of the obstruction or becomes completely disorganized, so that a chronic hydronephrosis is not produced. The production of chronic hydronephrosis by partial obliteration of the ureter is difficult and often complicated by infection. In any case the renal insufficiency associated with hydronephrosis is more or less a separate entity.

Production of Nephritis by X Rays.

It has been shown by various workers that renal insufficiency can be readily and consistently produced by this means. Of these Hartmann, Bolliger and Doub[4] are the only ones who have made functional studies throughout the course of the experimental disease, but their work was done by the rather uncertain technique of irradiating the kidneys through the abdominal wall with hard rays. In some cases numerous applications were required and the production of a standardized renal lesion was not obtained or even sought.

Object of Present Study.

The object of this investigation has been to obtain a technique by means of which a nephritis of a constant intensity and duration may be produced with certainty at any time. To obtain this result a series of experiments detailed below was performed, by means of which we did succeed in producing a more or less standardized lesion during the progress of which clinical and biochemical observations were made. This paper will be mainly concerned with a description from the clinical and biochemical aspects of the lesion we obtained.

Further, as an example of one of the uses to which a standardized nephritis may be put, we investigated the Andrewes diazo reaction in nephritis, with reference to its time of appearance, prognostic value and relation to other biochemical tests. On the details of these findings we shall report in a later communication.

Technique.

Dogs were used and were kept in semi-captivity under conditions which allowed them plenty of exercise and sunlight. Dogs operated on were kept in a special kennel during the night following operation, but after this received no special attention except when put for short periods into metabolic cages for purposes of special study. Their diet throughout consisted of cooked meat, scraps and water *ad libitum*, supplemented occasionally by raw meat and dog biscuits. The only preexperimental interference with the dogs was removal of the vocal cords of the majority with a punch.

The operative technique has been described in the previous paper. In brief, it consists in delivering one kidney on to the loin, either before or after opposite nephrectomy and exposing it to a measured dosage of X rays, this being in one series of animals about 3,800 international *r* units, in a second series

half that amount. This was obtained by giving 3·5 ampères at 112 kilovolts by a "Metalix" tube for periods of thirty and fifteen minutes respectively, no filters being used; the distance from the exposed kidney to the anticathode being 25·4 centimetres (ten inches). This dosage corresponds to about fifteen human erythema doses for the thirty minute exposure. Ether anæsthesia was mostly employed, after a preliminary injection of morphine, but for several animals "Avertin" was used with success.

Chemical Technique.

Blood.

For purposes of examination blood was withdrawn from the saphenous vein. It was examined for its urea content and for its hæmoglobin value. The technique used for the former was the urease method of Van Slyke and Cullen, described by Maclean.[5] In addition to this the simple and rapid method of Hensch and Aldrich[6] was frequently employed. For the estimation of the hæmoglobin value the Sahli method was used.

With the onset of renal insufficiency as indicated by a rising blood urea or in some instances before this, further investigations were carried out, determinations being made of the blood-creatinine content, the method of Myers[7] being used, the carbon dioxide combining power, estimated by the method of Van Slyke and Cullen,[8] Andrewes's diazo reaction in nephritis[9] and the cholesterol content of the blood by Myers and Wardell's method.[10]

Urine.

All available samples of urine were examined for specific gravity, albumin, cells, casts and doubly refracting bodies.

Several animals were put into metabolic cages and their 24-hour urine output and water intake measured during the greater part of the course of the disease.

The urea content of the urine was regularly determined.

Determinations of the phenolsulphonephthalein excretion were carried out in a certain number of animals.

Other aspects of nephritis, such as cardio-vascular changes, chloride, mineral and carbohydrate metabolism, were not investigated.

Results of Studies of Functional Changes in the Animals Subjected to Experiment.

As mentioned in the previous paper[1] the animals made use of fall into two separate groups. In the first group the kidney was exposed to X rays under the conditions mentioned for a period of thirty minutes; in the second for a period of fifteen minutes. The results obtained in the two groups differed so widely from one another that the first group only will be considered in this report; the second series being still under observation, will be reported on later.

The animals under present consideration can be further divided into two groups, according to the stage at which nephrectomy was carried out. In group A the animals received X radiation to one kidney followed by nephrectomy on the opposite side after a variable interval; in group B nephrectomy was carried out first, after which the remaining kidney was subjected to X irradiation.

GROUP A.

In Table I the results obtained in Group A are summarized, that is in those dogs which had the full standard dose of X rays, followed after a variable interval by opposite nephrectomy.

As the progress of the disease was found to vary according to two main factors, the interval allowed to elapse between the irradiation and the nephrectomy and the weight of the dog, this group can be conveniently further subdivided into three subgroups: (i) Dogs of medium or small size, on whom nephrectomy was carried out within forty days after irradiation, (ii) dogs of larger size, on whom nephrectomy was done up to fifty-one days after irradiation, (iii) dogs of all sizes when a comparatively long interval elapsed between the irradiation and nephrectomy.

We shall proceed now to describe the course of the experimental disease in these three groups in order, with reference to the clinical course, the blood chemistry, the urinary changes and the patho-

TABLE I.

Group A: Effect of X Radiation of One Kidney and Removal of the Other.

Dog.				Interval between Irradiation and Nephrectomy, Days.	Period of Survival after Nephrectomy, Days.	Total Life after Irradiation, Days.	Blood Urea at Death, Milligrammes.	Weight of Kidneys.	
Sub-Group.	Number.	Sex.	Weight, Kilograms.					Untreated, Grammes.	Treated, Grammes.
1	33	F.	7·7	9	30	39	563	27·7	18·9
	40	M.	9·5	9	22	31	600	26·9	21·0
	55	F.	6·8	20	15	35	558	23·7	22·2
	59	M.	6·5	20	14	34	293	23·7	23·5
	25	F.	5·2	24	6	30	405	25·0	10·4
	22	F.	4·3	36	4	40	420	20·9	9·15
2	54	F.	10·0	12	31	43	691	36·8	32·1
	53	M.	12·3	15	30	45	514	40·3	40·4
	3	M.	12·7	31	19	50	558		
	8	M.	20·0	51	134	187	Recovered	72·0	80·0
3	16	M.	13·2	57	3	60	286	60·0	11·6
	13	M.	5·9	60	3	63	290	18·6	10·0
	15	M.	7·3	71	4	75	505	50·8	10·4
	17	M.	13·2	87	3	90	234	52·5	8·2
	2	M.	10·5	45	3	48	343	44·0	23·0
	12	M.	17·7	104	4	108		32·0	10·0

logical findings. The latter which have been fully described in a previous article, will only be enumerated briefly.

Subgroup 1.

Subgroup 1 comprises six dogs whose body weight ranged from 4·3 to 9·5 kilograms. The interval between the irradiation and the removal of the opposite kidney ranged from nine to thirty-six days.

The dogs in this group made good recoveries from both operations. There is naturally some associated loss of weight which is not at first very evident. The first feature of note observed is that this loss of weight is not made up as would be expected.

Apart from this there is no change in the dog's condition during the first three weeks; it is lively and active and eats well. After this, however, various changes occur, usually within a very short time. The dog sporadically loses interest in its food and wasting becomes more pronounced. There is frequently at this stage a slight temporary gain in weight, which would not be expected from consideration of the animal's state of nutrition. We consider that this is due to œdema. This condition is often quite evident clinically, being repeatedly observed around the eyes and in the feet and genitals. At this period the animal is very thirsty and measurement of the water intake and urine output shows a considerable discrepancy, the water retention in some cases being as high as one litre in twenty-four hours. Pallor of the mucous membranes is commonly observed. Later dehydration occurs, the animal becomes extremely weak, commences to vomit the small amount of food eaten and sometimes refuses food altogether. Following this muscular twitchings, especially of the head muscles, are observed, dyspnœa becomes a prominent feature and death ensues between thirty and forty days after irradiation, preceded in some instances by a period of coma. In the later stages itchiness of the skin is observed in the majority. The course of the disease in some dogs departs somewhat from this general description; some go progressively downhill, others remain in fairly good condition till signs of uræmia suddenly appear.

Chemistry of the Blood.

Urea.

In Chart I the urea content is given of the blood of the dogs of this group throughout the course of the disease. During the interval between the irradiation and the nephrectomy, there being a normal kidney present which will compensate for

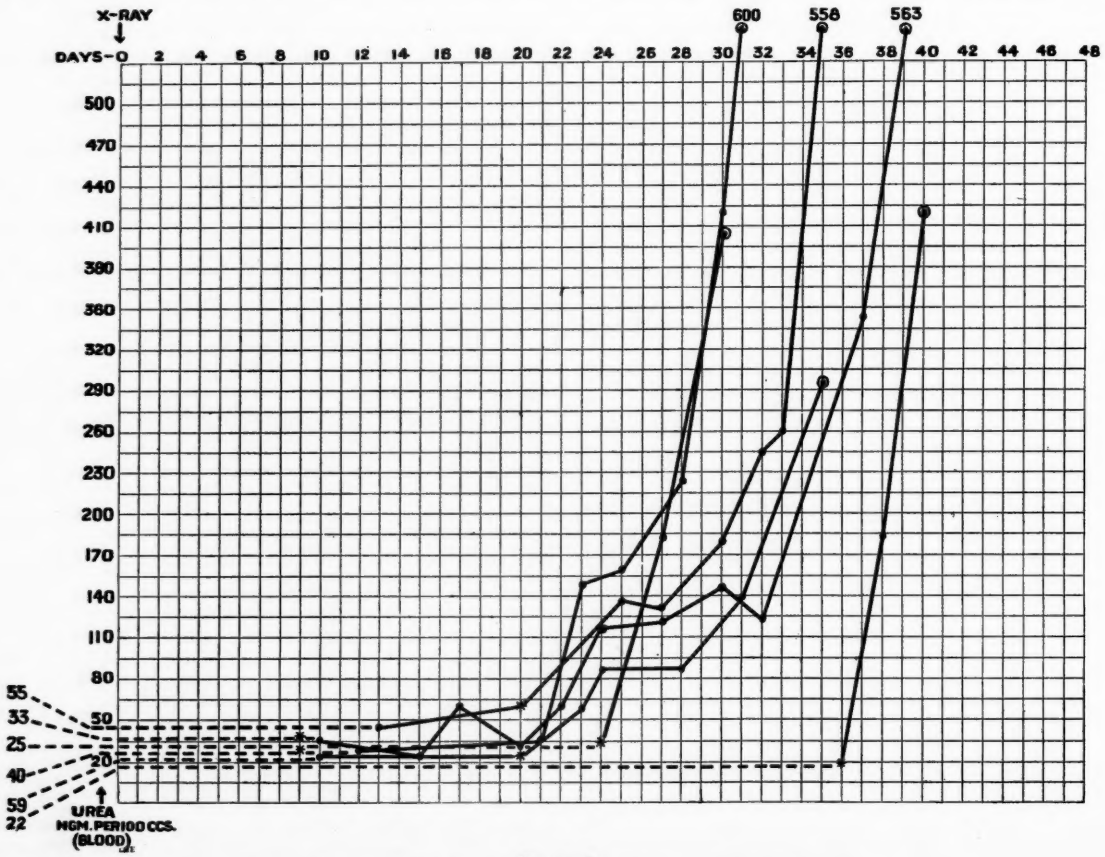

Chart I.
Group A. Irradiation followed by nephrectomy on the opposite side.
* = nephrectomy. ⊙ = death.

any defect in its fellow, no considerable changes can occur. After nephrectomy, however, the picture is different. About three weeks after irradiation a steady rise commences. By the end of the fourth week in most of the dogs the value is well above one hundred milligrammes per hundred cubic centimetres and rises inevitably from this point till death occurs in the fifth or early in the sixth week, when maximum values are recorded, in practically every animal above four hundred milligrammes.

Creatinine.

Coincident with the rise in the urea there is some increase in the creatinine content of the blood. This, however, is not great till the terminal stages are reached, when it rises to a maximum value, usually above six milligrammes per hundred cubic centimetres of blood.

Carbon Dioxide.

The carbon dioxide combining power undergoes no change during the first three weeks, while the urea content of the blood remains normal. Simultaneously with the rise in the urea, however, the carbon dioxide combining power of the plasma diminishes, the diminution becoming extremely serious as the terminal stage is reached, coincident with the clinical sign of dyspnœa which is noted in these animals. Values below 10% are constantly met with.

Cholesterol.

The cholesterol values before removal of the untreated kidney varied from one hundred to one hundred and fifty milligrammes per hundred cubic centimetres, averaging about one hundred and ten milligrammes. From three to four weeks after irradiation, provided the other kidney has been removed, the values begin to rise. This period coincides with the occurrence of fatty changes in the irradiated kidney as described in the previous article.[1] From this point up till death the readings were found to lie between one hundred and eighty and three hundred and forty milligrammes per hundred cubic centimetres.

Andrewes's reaction will be referred to later.

Hæmoglobin.

A good many routine hæmoglobin estimations were made. Some degree of anæmia was invariably present in the course of the disease, a fall occurring in the hæmoglobin value, the difference between the value at death and that at the time of the exposure to X rays ranging up to 20%. In some cases a terminal increase was noted, corresponding apparently with the extreme dehydration present.

Urinary Changes.

A mild urinary infection, manifested by occasional pus cells and motile organisms seen by the microscope, was found to be present in many of the dogs examined and was probably associated with the frequent catheterization of the females, which supplied a large number of the specimens used in the investigation.

Findings associated with the experimental disease were as follow:

Albumin and Casts.

Albuminuria was found in all animals. It commenced in practically every dog immediately after irradiation, but at this stage was very slight in amount. It did not become severe as a rule till late in the disease, though in the urine of one dog a large quantity of albumin was present on the twenty-sixth day; death occurred on the thirty-fifth day. In the other five there was a faint cloud until a late stage, the amount being so small as to make it questionable whether or not it was secondary to the mild urinary infection present. From three days before death to the final termination, very severe albuminuria was uniformly present, out of all proportion to the degree of pyuria when this latter occurred.

Routine microscopical examination disclosed occasional red cells and casts, mostly of the granular variety. The number of casts found was not as copious as would be expected from a consideration of the severity of the lesion and in the majority of the experiments they were not found till a short period before death and then not in abundance. Examination with the polarizing microscope revealed in the latter part of the disease, commencing from three to four weeks after irradiation, the presence of doubly refracting bodies.

Volume.

The operative procedures involved in the production of the experimental disease naturally would have a temporary influence on the twenty-four hour urinary excretion, consequently this aspect was not studied till the dogs had recovered from the operation and urinary secretion was more or less stabilized.

It was found that diuresis was a distinct feature of the disease. By the end of the third week the output may be as high as 1,400 cubic centimetres, with a specific gravity of 1012, rising to three litres or more with about the same specific gravity or slightly less by the end of the fourth. From this stage the amount secreted fluctuates to some extent, but is mostly one and a half litres or over, till the final stages when an abrupt fall takes place, starting a few days before death. Values as low as forty cubic centimetres the day before death were met with, but accurate estimation was not possible owing to contamination with vomitus. Complete anuria was not met with except during the last few hours of life.

Urea Excretion.

The percentage of urea in the urine varied a good deal. Direct comparison of the results obtained with the findings met with in the human subject cannot be made, as the normal concentration of urea in the dog is possibly higher than that

encountered in man (Antoine and Liégeois[11]). Pathological figures in the dog are as far as we are aware not yet known. If this is borne in mind, the values obtained by simply estimating the percentage of urea in the urine will be seen to correspond quite closely with other aspects of the disease. Urea concentration tests proper were not carried out, as the administration of urea to dogs is tedious, a stomach tube having to be used and the urea is frequently vomited. Moreover, in the later stages the urea content of the blood is much elevated, making any artificial increase of this unnecessary.

During the period of polyuria, low values are encountered, the lowest we recorded being 0·8%, the blood urea at this time being sixty-two milligrammes per hundred cubic centimetres. During this period it was always below 2%. As the urinary output drops and the urea content of the blood rises, the urea content of the urine may rise also, but not proportionately. Values above 2% are mostly met with in the final stage, the lowest value at this period being 1·2% and the highest 4%. In other cases there is little change till the few days before death, when there is a terminal slight rise.

Phenolsulphonephthalein Excretion.

The phenolsulphonephthalein excretion was examined in a few instances. It was found to be slightly depressed (50% to 60% in two hours) in the polyuria stage, diminishing rapidly with the rapid increase in the urea content of the blood and becoming practically nil in the terminal stage.

In Table II the detailed findings during the course of the disease in dogs A55 and A59 are given (see page 346).

Pathological Changes.

A detailed autopsy was performed as a routine and the absence established in each case of any cause of death other than the renal lesion.

The irradiated kidney at death was found in each case to be slightly smaller than its normal fellow removed at operation, the difference in weight varying somewhat with the length of the interval between radiation and nephrectomy.

Routine histological examination of the treated kidney in every animal revealed the picture associated with the period of tubular destruction and fatty change described in the previous article with the presence of anisotropic bodies as demonstrated by the polarizing microscope. The changes were confined to the cortex, where formation of fibrous tissue was also commencing. Small areas of early repair were occasionally visible. Except in one specimen mentioned in the previous paper the glomeruli were normal.

Figure I illustrates the gross appearance of the treated and untreated kidneys as seen in dog A40 and demonstrates the slight difference in size.

Summary for Subgroup 1.

Subgroup 1 comprises six dogs of medium size, of body weight of 9·5 kilograms and below, on whom nephrectomy was carried out at a comparatively early stage before the lesion in the irradiated kidney had progressed so far that the kidney would be unable by itself to maintain life. At a critical period, varying between thirty and forty days, the animals all died in the same condition, namely uræmia, accompanied by definite clinical, blood and urinary changes, irrespective of the date of removal of the good kidney. In every case renal insufficiency was proved by autopsy to be the sole cause of death.

It may be well to mention that Dog 22, included in this group, differs from the other members in that nephrectomy was delayed till the thirty to forty day period. The dog died from renal insufficiency on the fortieth day, proving that the irradiated kidney could not support life alone after this stage. That death would have occurred in the thirty to forty day period had nephrectomy been carried out earlier was not demonstrated, but it is at least highly probable.

Subgroup 2.

Subgroup 2 consists of four dogs which, however, were all of higher body weight than those included in the first group. As seen from the table their body weights ranged from ten to twenty kilograms and the interval between the irradiation and the nephrectomy varied from twelve to fifty-one days.

The behaviour of these four dogs differed from that of the previous group in that none of them died within the thirty to forty day period. Three of them died at periods up to fifty days after irradiation; the remaining one recovered. The first three dogs weighed respectively 10·0, 12·3 and 12·7 kilograms. The intervals between the irradiation and the nephrectomy were respectively twelve, fifteen and thirty-one days and death occurred forty-three, forty-five and fifty days after irradiation.

Clinically in these three dogs uræmic symptoms were later in development and the same statement may be applied to the blood and urinary changes. Chart II demonstrates the rise in the urea content of the blood of the dogs of this group as well as of a dog in Group B which will be discussed below. With the exception that the disease following on the irradiation was delayed and prolonged, their behaviour was in no wise different from that of the previous subgroup. The urea and creatinine content of the blood rose, gradually at first, more abruptly towards the finish, the carbon dioxide combining power dropped in the same manner; the same period of polyuria was present, the presence of albumin, casts, and doubly refracting bodies was noted and the animals became somewhat anæmic. We are confident that the explanation of the longer duration of life in these dogs lies in their comparatively high body weight and consequent high kidney weight as compared with those in Subgroup 1, so that the amount of renal damage sustained as a result of the exposure to X rays was slightly less than before and the kidney after opposite nephrectomy was able to sustain life for a slightly longer period.

In these dogs again routine autopsy disclosed no cause of death other than the renal lesion and

microscopical examination of the exposed kidney revealed the same features of tubular destruction and fatty change as before. The only difference was that the formation of fibrous tissue and the attempts at tubular repair were rather more evident.

The fourth dog, A8, in the subgroup demonstrates the same features, but to a much greater extent. This dog was a strong animal of twenty kilograms body weight. A period of fifty-one days was allowed to elapse between the irradiation and the nephrectomy after which the irradiated kidney in a dog of smaller size, judged from the standard set by the animals of Subgroup 1, should be totally unable to maintain life. Following nephrectomy there was a steady rise in the blood urea which reached a value of 112 milligrammes sixteen days after operation. There was then a fall, the value being 54 milligrammes eleven days later, and after this followed a period of about two months during which the value was mostly between 80 and 100. There was a further fall at this stage, the urea content being 51 milligrammes per hundred cubic centimetres 134 days after nephrectomy, that is 187 days after the irradiation. At this period the animal was killed. Clinically it had remained in good condition during the whole course of the disease. The irradiated kidney removed at autopsy was found to be greatly hypertrophied; it weighed eighty grammes. The other kidney, removed fifty-three days after the irradiation and therefore itself almost certainly hypertrophied to some extent, weighed seventy-two grammes. Microscopically the prominent feature of this kidney was the extensive tubular repair present, all tubules seen being large, healthy looking and hypertrophied. Small wedges of fibrous tissue were present, proceeding down from the capsule into the cortical region.

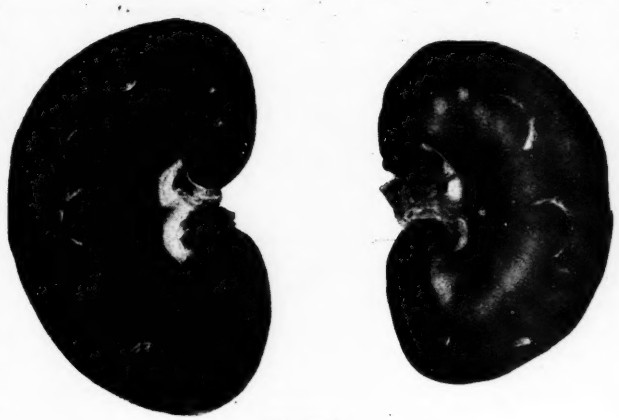

FIGURE I.

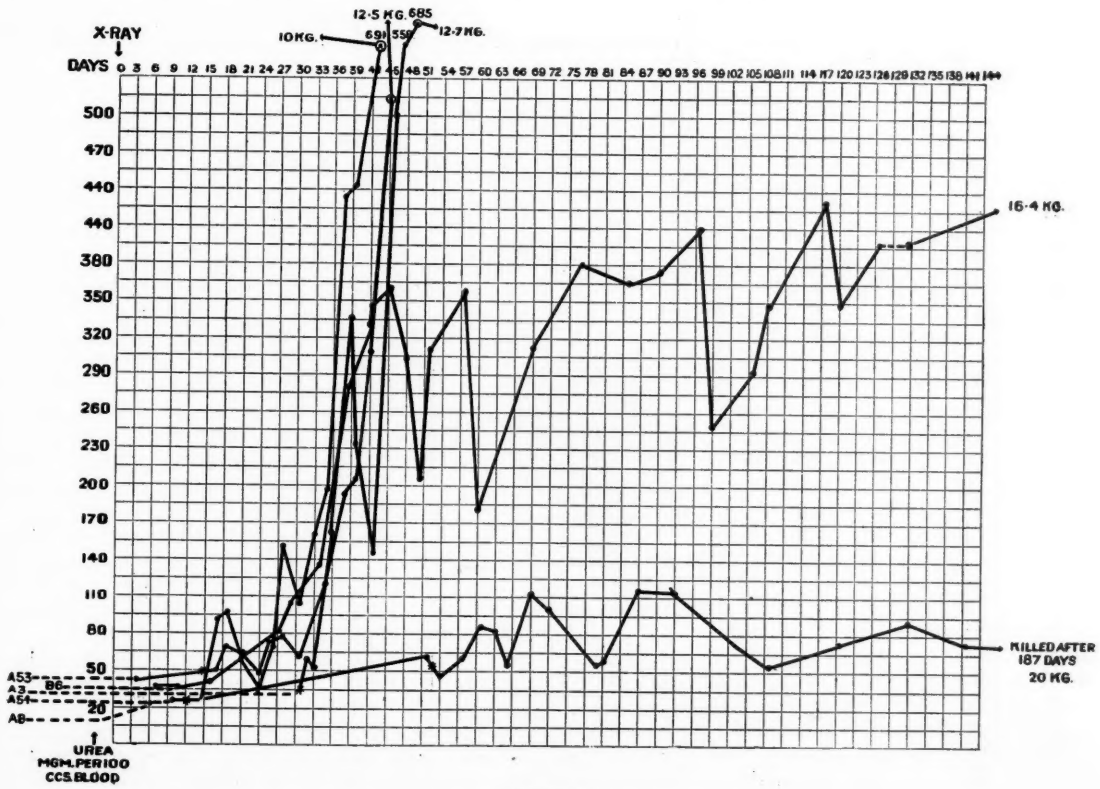

CHART II.
Animals of groups A and B which survived over the forty-day period.

TABLE II.

Studies of the Functions of Dogs A55 and A59.

Dog.	Day.	Blood.						Urine.				
		Urea, Milligrammes per 100 Cubic Centimetres.	Creatinine, Milligrammes per 100 Cubic Centimetres.	Andrewes's Reaction.	Cholesterol, Milligrammes per 100 Cubic Centimetres.	Carbon Dioxide Combining Power. %	Hæmoglobin. %	Specific Gravity	Albumin.	Casts.	Urea. %	Excretion 24 Hours, Cubic Centimetres.
A55	13	47	—		—	—	60	—			—	—
	20	61	—		—	—	—	—			—	—
	23	75	3·0	–	—	36	—	—			—	—
	25	138	—		—	—	41	—			—	—
	26	—	—		—	—	—	—	+++		1·9	800
	27	120	—	–	—	26	—	1018	++		—	—
	30	178	—	–	—	—	—	—			—	—
	32	245	—	+	—	—	45	—			—	—
	33	260	—	++	—	—	42	—			—	—
	35	558	4·0	+++	—	7	—	—	+++		—	—
A59	13	25			100	—	—	—			—	350
	23	59		–	200	—	—	—			—	1,150
	24	87		–	198	—	55	—	+		—	—
	28	88		–	180	—	—	—			—	—
	30	—			—	—	44	1015	++		1·75	—
	31	139		–	186	—	—	—			1·32	1,050
	32	—			—	—	—	—			1·21	1,200
	33	—			—	—	—	—			1·46	600
	34	293		+++	262	—	—	—			2·15	200

In Table III the detailed findings during the course of the disease in dogs A53 and A54 are given.

Summary for Subgroup 2.

In contrast to those of the previous group the four animals in Subgroup 2 with relatively high

TABLE III.

Studies of the Functions of Dogs A53 and A54.

Dog.	Day.	Blood.					Urine.					
		Urea, Milligrammes per 100 Cubic Centimetres.	Creatinine, Milligrammes per 100 Cubic Centimetres.	Andrewes's Reaction.	Carbon Dioxide Combining Power. %	Hæmoglobin, %	Specific Gravity.	Albumin.	Casts.	Urea. %	Excretion 24 Hours, Cubic Centimetres.	Phenolphthalein Excretion. %
A53	4	43	—		—	—	1013			—	900	
	5	—	—		—	—	—			—	1,000	
	6	—	—		—	—	—			—	—	
	15[1]	—	—		—	—	—			—	—	
	17	50	—		—	—	—			—	—	
	19	68	—		—	50	—			—	—	
	21	64	—		32	46	—			—	—	
	24	48	—		—	—	—			—	—	
	25	—	—	+	—	—	—	+	+	—	—	
	26	70	—	+	—	54	1011	+	+	1·0	1,700	
	27	—	—	+	—	—	1011	+	–	0·82	2,500	
	28	79	—	–	—	—	—	–	–	0·72	3,000	
	29	—	—		—	—	—			—	2,500	
	31	62	—	–	27	—	1007	+		0·65	1,750	
	32	—	—	–	—	—	—	–		0·9	2,300	
	33	—	—		—	52	1010	–	–	1·02	3,100	
	34	—	—		—	—	—	+		1·0	2,000	
	35	121	2·5	–	22	—	1010	+	–	—	—	
	38	192	—	+	—	—	—			—	—	
	40	204	—	+	—	51	1012	+	+	—	—	
	41	—	—		—	—	1016	+	++	1·55	—	
	42	296	—	+++	—	—	—			—	500	
	45	514	4·8		—	—	—			1·6	—	
A54	10	27	—		—	54	—			—	—	
	12[1]	—	—		—	—	—			—	—	
	14	27	—		—	—	—			—	—	
	17	93	—		—	—	—			—	—	
	19	96	2·4	–	—	—	—			—	—	54
	21	58	—		—	50	1012	+	–	—	1,400	
	22	—	—		—	—	—	+	+	—	1,200	
	24	36	—		—	—	1009	+	–	—	1,100	
	25	—	—		—	—	—			—	1,500	
	26	67	—	–	—	—	1013	+	+	0·72	2,500	
	27	—	—		—	—	1012	+	–	0·8	2,800	
	28	152	—		—	—	—			—	3,800	
	29	—	—		—	—	—			—	2,700	
	31	106	3·0	–	12	—	—			—	2,000	50
	32	—	—		—	—	—			—	2,200	
	33	162	—		—	51	1012	+++	+	1·3	2,300	
	34	—	—		—	—	—	++		1·65	1,800	
	35	198	—	–	12	—	1016	+	+	—	—	
	36	—	—		—	—	—			—	1,200	
	38	430	—		—	—	—			—	—	
	40	441	—	++	8	45	—	+++	+	—	—	7
	42	490	—	+++	—	—	—	+++	+	1·45	400	
	43	691	4·1	++	—	—	—	+++		1·3	30	

[1]Nephrectomy performed. On the 19th day the cholesterol content of the blood of A54 was 130 milligrammes per hundred cubic centimetres.

body weights survived longer. Three of them died at intervals ranging from forty-three to fifty days after irradiation, in the order of their body weights. The remaining one, by far the largest dog in the group, survived indefinitely. We feel assured that the explanation of this lies in the fact that the larger amount of kidney substance present sustained less damage than in the dogs of the previous group, enabling life to be carried on past the forty day period to an extent varying directly with the weight of the dog.

Subgroup 3.

Subgroup 3 contains six animals and proves further the points brought out in the previous groups, that in the average animal as used in our experiments the irradiated kidney is unable to maintain life after a certain definite period. In these dogs after periods ranging from 45 to 164 days after the irradiation the good kidney was removed and every animal died with clinical signs and laboratory evidence of renal insufficiency within a period of four days. Two animals were as far as weight is concerned in the same class as those of Subgroup 1, the remaining four would have fallen into Subgroup 2. In each instance the good kidney was removed at a later date than was the case in the corresponding subgroup and in each instance the fact was brought out that the lesion had progressed too far to allow of life being carried on after opposite nephrectomy by the diseased kidney alone. Even in one animal of 17·7 kilograms body weight the same observation was made, the explanation being that the interval (in this animal 104 days) between the irradiation and the nephrectomy was sufficient to allow complete disorganization of the treated kidney. This is shown by the fact that the treated kidney weighed only sixteen grammes at autopsy and apart from one fair sized area of regeneration there was histological evidence of almost complete destruction of the tubular apparatus. The other kidney, removed at operation, weighed fifty-four grammes. In dog number 8 of the previous subgroup, a dog of slightly larger size which survived, the good kidney was removed after fifty-one days, while there was not yet sufficient renal damage to prevent the kidney from supporting life. We feel confident, however, that had the period between the two operations been longer, for example one hundred days, this dog also would have met with the same rapid fatal termination.

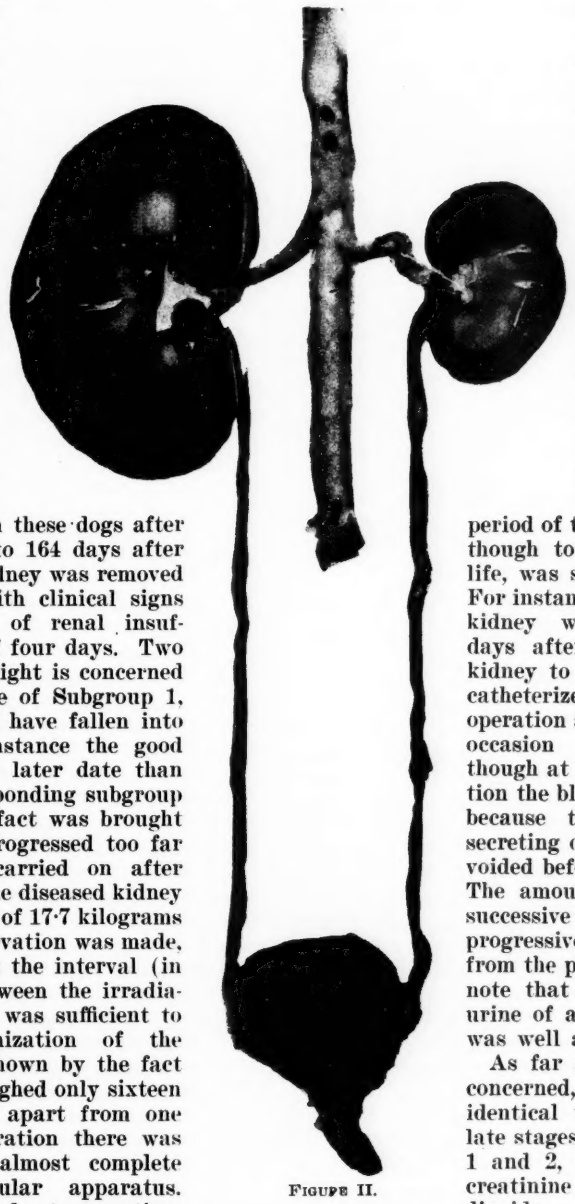

Figure II.

As pointed out, all the animals in this subgroup died three or four days after nephrectomy. Most of them appeared to be well the day after operation. On the following day usually a definite rise in the urea content of the blood was noted and uræmic symptoms were observed, consisting in vomiting, anorexia and thirst, as observed previously. Some drank large quantities of water, the greater part of which was vomited. In others the fluid intake was small and in these animals particularly dehydration became evident. Most of the dogs were observed to void urine after operation and a bladder full of urine was a common finding *post mortem*, showing that even after a long period of time the irradiated kidney, though totally unable to maintain life, was still secreting some urine. For instance, in dog A15 whose good kidney was removed seventy-one days after exposure of the other kidney to X rays, the bladder was catheterized immediately after operation and thence daily. On each occasion urine was withdrawn, though at the *post mortem* examination the bladder was empty, whether because the kidney had stopped secreting or because the animal had voided before dying, cannot be said. The amount of urine obtained on successive days, however, became progressively less. It is interesting from the physiological standpoint to note that the urea content of the urine of all the dogs in this group was well above 2%.

As far as functional studies are concerned, the findings were identical with those found in the late stages in the dogs of Subgroups 1 and 2, that is a high urea and creatinine content, a low carbon dioxide combining power and Andrewes's reaction. Albuminuria was present. Before operation the renal function of these dogs was either perfectly normal or very close to normal, according to whether or not full compensatory hypertrophy of the sound kidney had had time to take place.

Macroscopically the differences in size in each case

between the treated kidney and its normal fellow previously removed were very striking and are demonstrated in Figure II. Histologically the treated kidney invariably showed almost complete tubular destruction with advanced fibrosis, the glomeruli on the other hand being more or less normal. A full description has been given in the previous paper.

Summary for Subgroup 3.

Subgroup 3 consists of six dogs with widely varying body weights. Comparatively long periods were allowed to elapse between the irradiation and nephrectomy, by which time the irradiated kidney was totally unable to support life. In each animal death from renal insufficiency occurred within four days.

GROUP B.

Group B, as mentioned above, consists of animals which had nephrectomy followed after a variable interval by irradiation. The interval varied from six to forty days. In Table IV the weights of the dogs are set forth and the course of the disease is briefly indicated.

These dogs can be divided into subgroups as before according to body weight. The first subgroup consists of four animals with body weights ranging from 6·2 to 8·6 kilograms, the second of one animal only, weighing 16·4 kilograms.

Subgroup 1.

In the four dogs of Subgroup 1 the interval between nephrectomy and irradiation varied from six to forty days; all four died at a period ranging from thirty to thirty-nine days after irradiation with all the symptoms of uræmia and with renal insufficiency being proved by autopsy to be the sole cause of death. Chart III demonstrates the behaviour of the blood urea in these four animals. During the first week after irradiation the urea content of the blood remained at a normal level. During the second week there was noticed a tendency for the value to rise, but in no case did the elevation reached exceed a value of eighty milligrammes. The values in the third week again were much the same as in the second. In the fourth week values of about one hundred and forty milligrammes were the rule. From this point the rise became more abrupt and in the fifth or early in the sixth week the urea content reached its maximum value at death of about five hundred milligrammes or more. In the light of our experiences with Group A it was not considered necessary to repeat the detailed investigations already carried out on other aspects of the disease. The occasional tests that were done agreed with the findings of Group A, for instance the usual low carbon dioxide combining power was met with and albuminuria was again present in the later stages.

Clinically again the same train of symptoms was observed as in Group A.

Subgroup 2.

The sole member of Subgroup 2 was a full-grown, young, healthy male weighing 16·4 kilograms. A period of thirteen days elapsed between the nephrectomy and the irradiation. The kidney removed at operation weighed sixty-four grammes and that exposed at the time of the irradiation appeared to be approximately the same size. The dog survived for 131 days after irradiation before dying from renal insufficiency.

For the first three weeks the behaviour of the urea content of the blood was about the same as in the previous subgroup and can be seen in Chart II. After this, however, the rise was not so acute, the value gradually rising to 360 in the middle of the seventh week. After this, except for a few fluctuations when it temporarily dropped to values in the neighbourhood of 200, it remained well above the 300 mark till death. The maximum value recorded was 430 milligrammes on the one hundred and eighteenth day. The last estimation was made four days before death and yielded a value of 397 milligrammes.

Creatinine estimations were carried out during the latter half of the disease. The values ranged from 3·3 to 5·9 milligrammes and the carbon dioxide combining power over the same period ranged from 22% on the eighty-fifth day to 9% four days before death. During the same period Andrewes's reaction was always obtainable.

A striking feature of the disease in this dog was a very severe anæmia. The hæmoglobin value of the blood by the sixty-ninth day had dropped to 24%. The highest reading obtained on any occasion subsequent to this was 32%.

Albuminuria was as usual found to be present and a few casts were found from time to time. A considerable degree of polyuria was present during the latter half of the disease, the quantity of urine reaching up to 1·7 litres in twenty-four hours. The

TABLE IV.

Group B: Effect of X Radiation of One Kidney and Removal of the Other.

Dog.				Period between Nephrectomy and Irradiation, Days.	Period of Survival, Days.	Blood Urea at Death, Milligrammes.	Weight of Kidneys.	
Sub-Group.	Number.	Sex.	Weight, Kilograms.				Untreated, Grammes.	Treated, Grammes.
1	1	F.	6·8	40	31	693	—	—
	4	M.	6·2	10	37	504	24·8	22·0
	8	F.	7·3	6	39	640	25·1	24·1
	9	F.	8·6	13	30	495	24·0	27·0
2	6	M.	16·4	13	131	397	64·0	33·0

excretion dropped as usual during the last few days, being only one hundred cubic centimetres on the day before death.

Clinically the animal showed progressive loss of weight, weighing only 11·1 kilograms four days before death. It ate well up till a few days before death, but had a good deal of weakness and loss of energy. Vomiting occurred for a few days before death. The animal died during a week-end and its termination was not observed.

The pathological picture of this dog has been fully described in the previous paper.[1] The macroscopic appearance of the kidneys is seen in Figure III. In Table V the blood chemistry and urinary findings during the latter half of the disease are set out.

As in Group A2, the greater chronicity of the disease in this dog would appear to be due to its comparatively high body weight and associated high kidney weight, resulting in less renal damage.

CASES IN WHICH THE RENAL LESION DID NOT PURSUE ITS CUSTOMARY COURSE.

Throughout the series of animals in which experimental nephritis was produced, there were three only whose behaviour in the light of our experiences over our fairly large series was different from what we had expected. All three animals developed renal insufficiency and all died, but not at the expected period. Satisfactory explanations, however, were forthcoming, in the shape of unforeseen factors complicating the nephritis, as would indeed be inevitable in a series of dogs of sufficient number. One animal belonged to Group A and the other two to Group B. We shall report on these animals in some detail.

Dog B5 was a female weighing 7·9 kilograms. During the delivery of the kidney for the purpose of exposing it to X rays ten days after nephrectomy, the peritoneal cavity was inadvertently opened and it was noticed that the cornu of the uterus on that side, which in the bitch extends up to the lower pole of the kidney, was definitely enlarged, the condition apparently being one of moderately advanced pregnancy. It is well known that in the presence of severe nephritis pregnancy is a serious complication. In the bitch in question the first blood urea estimation was carried out three days after the irradiation, when the value was already found to be 228 milligrammes. During the next fourteen days the animal's condition remained good and the wound healed by first intention. No further rise in this period took place in the blood urea which was 178 milligrammes per hundred cubic centimetres on the seventeenth day. On the eighteenth day the animal came into labour, which condition lasted for

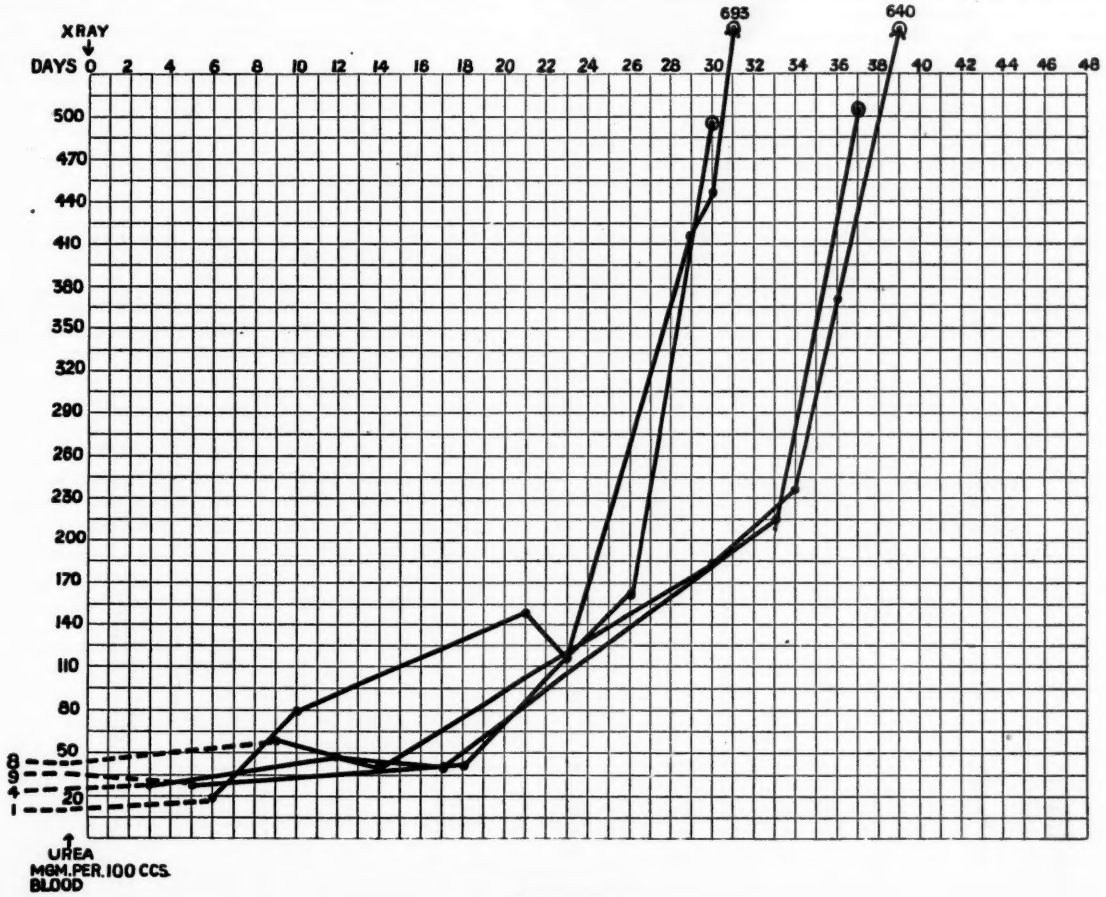

CHART III.
Group B. Nephrectomy followed by irradiation.

two days. Two puppies only were born, both of large size and both were stillborn. During the period of labour on the nineteenth and twentieth days, the blood urea was 413 and 405 milligrammes per hundred cubic centimetres respectively. On the twenty-first day the animal was weak and exhausted, with much dyspnœa and was found dead next morning. It is advisable to point out that there was no evidence of previous nephritis in this animal. The kidney removed at operation was normal both macroscopically and microscopically and the other organ delivered on to the loin for exposure to X rays was also normal in size and macroscopic appearance. It would appear that the complicating advanced pregnancy was responsible for the unusual severity of the disease.

Dog B12 was a male, weighing 13·4 kilograms. Irradiation was carried out in the usual way three days after nephrectomy. From previous experience this animal would have been expected to live for more than the forty day period. As early as two days after operation, however, it was noticed that the animal had some pyrexia and did not eat. The condition improved to some extent, but the animal did not recover completely. For the first three weeks after the irradiation there was no distinct elevation of the blood urea which was sixty-one milligrammes on the twenty-third day. On the twenty-eighth day it was eighty-six milligrammes and 186 on the thirtieth. At this stage the animal commenced to vomit and died next day with a urea content of its blood of 296. *Post mortem* abscesses of the lower lobes of both lungs were found.

Dog A60 was a male, weighing seven kilograms, which had the usual dose of X rays followed twenty-two days later by nephrectomy. The animal died from renal insufficiency on the forty-first day, though from a consideration of its body weight death should have occurred between thirty and forty days. There was no complicating disease.

FIGURE III.

The interesting feature of this dog, however, was the fact that the good kidney, removed twenty-two days after irradiation, by which time some hypertrophy should be present, weighed 22·3 grammes, while the irradiated kidney at autopsy weighed 24·5 grammes, over two grammes more.

In every member of Group A1 the treated kidney weighed less than its fellow and we are inclined to attribute the abnormal behaviour of this dog to the fact that the renal tissue was probably not evenly distributed between the two kidneys, the treated kidney being the larger and not sustaining the expected amount of damage. This hypothesis is supported by the fact that at the time of the irradiation it was noticed that this kidney was abnormally large for the weight of the dog.

In conclusion we wish to mention that all the other dogs, a considerable number, which have not been described in this paper, were either killed and investigated from the histological standpoint only or died from intercurrent infection after the first operation. Every dog that survived both operations, has been reported on.

DISCUSSION.

The Rôle Played by Factors Other than Irradiation in the Course of the Experimental Disease.

Body Weight.

Over a large series of animals we have produced a renal lesion in every animal by means of the

TABLE V.

Studies of the Functions of Dog B6 during the Latter Half of the Experimental Disease.

Dog.	Day.	Blood.					Urine.					
		Urea, Milligrammes per 100 Cubic Centimetres.	Creatinine, Milligrammes per 100 Cubic Centimetres.	Andrewes's Reaction.	Carbon Dioxide Combining Power. %	Hæmoglobin. %	Specific Gravity.	Albumin.	Casts.	Urea. %	Excretion 24 Hours, Cubic Centimetres.	Weight, Kilograms.
B6	77	380	—		—	23	1017			—	1,700	12·3
	78	—	3·9		15	24	1021	+++	+	2·75	850	—
	79	—	—		—	—	—			—	1,050	—
	80	—	—		—	—	—			—	1,250	—
	82	—	—		—	—	—			—	1,050	—
	84	—	—		—	—	—			—	750	—
	85	365	—	+	22	26	—			—	880	—
	86	—	—		—	—	—			—	850	—
	90	373	—	+	17	28	—			—	—	—
	91	—	—		—	—	1020			—	1,400	—
	92	—	—		—	—	—			—	940	—
	94	—	—		—	—	—			—	850	—
	95	—	—		—	—	—			—	1,250	—
	97	410	5·9	++	32	32	—			—	—	—
	99	268	—	+	—	—	—			—	—	11·8
	106	292	3·3		—	—	—			—	—	—
	108	343	3·25	+	—	32	—			—	—	—
	118	430	—		—	—	—			—	—	11·1
	120	348	4·4		—	28	—			—	—	—
	127	397	—	+	9	28	—			—	—	11·1
	128	—	—		—	—	1010	+	+	—	—	—
	129	—	—		—	—	—	+++	+	2·2	150	—
	130	—	—		—	—	—	+++		—	100	—

Death occurred on the 131st day.

technique described, using a constant heavy dosage of X rays. Various degrees of renal damage were produced, the effects varying from death within a period of thirty to forty days in animals of medium size, up to ten kilograms, to almost complete recovery in large dogs. In animals of intermediate size, up to 12·7 kilograms, death occurred after the forty day period. In other words, the severity and duration of the disease varied directly with the weight of the dog, as influencing the size of the kidney exposed to X rays and determining in consequence the amount of renal damage sustained.

Renal Counterbalance.

One would expect from a study of the principles of renal counterbalance that the date of removal of the sound kidney would be a large factor in the course of the disease. We found that this was not the case, whether nephrectomy was carried out some time before irradiation, thus providing a greater stimulus to the damaged kidney to resist the interference with it, or whether it was deferred for a period of anything up to thirty days after irradiation, giving ample encouragement to the treated kidney to offer no resistance to the damage, there being a sound kidney to support life, the clinical and biological results were practically what would be expected from a consideration of the body weight alone. The reasons for this will be discussed in the next section. The action of the laws governing renal counterbalance becomes apparent later when the treated kidney in the continued presence of its healthy fellow becomes more and more completely disorganized.

Operative Procedures.

In Group B, where the nephrectomy is done beforehand and the disease does not become acute for over three weeks after the irradiation, sufficient time elapses for good healing of both wounds, which in all the dogs was satisfactory by the time urea retention was noticed. In Group A, on the other hand, in those animals in whom nephrectomy was performed comparatively late and urea retention appeared immediately after operation, the healing of the wounds was at times unquestionably delayed, the delay being almost certainly due to the depressed general condition of the dog and consequent susceptibility to infection. In the event of undoubted infection free drainage was provided. In no instance did the course of the disease in the presence of wound infection differ materially from that observed where healing took place by first intention. In other words, although in some dogs the renal lesion exerted an unfavourable influence on the operation wounds, the operative procedures appeared to exert little, if any, influence on the course of the disease.

Similarly other factors, such as constitution, sex, season, age, do not come into play to any large extent. The severity of the renal lesion and its uniformity overshadow all outside factors save the weight of the dog, which really means the size of the kidney exposed to X rays. Fallacies are, of course, possible, since the relation of the kidney weight and body weight was found to vary to a certain extent. Moreover, there is an additional potential basis of error in those animals in whom the two kidneys show considerable congenital differences in size, as encountered by us in the dog A60.

A Standardized Renal Lesion.

The ten animals comprising Group A1 and B1 after exposure of the life-supporting kidney to the standard dosage of X rays died at a period between thirty and forty days from renal insufficiency. The clinical and functional studies made reveal the remarkably uniform course of the disease. The observations made during the first three weeks after exposure hardly indicate the severity of the reaction which takes place in the following weeks, urea retention during this former period, if any, being slight. In the later stages urea retention is considerable. Albuminuria is present in varying degree, but becoming more evident towards the end. The cholesterol content of the blood is distinctly and consistently elevated. Up to the very last days polyuria is present and the urea concentration of the urine is low. Anisotropic bodies are present in the urine. Clinically there is slight and fluctuating œdema. Loss of weight is considerable. Death is definitely uræmic. The glomeruli are remarkably well preserved and no striking changes were seen, with one exception already mentioned in the article on the histological changes.(1) The tubules have undergone fatty degeneration and necrosis. Anisotropic bodies are present. Evidence of early attempts at repair is always visible and there is early formation of fibrous tissue.

The only material departure from the uniformity of the series is dog A40, an animal of 9·5 kilograms body weight which survived only thirty-one days. One would have expected this dog, being the largest in the group, to have survived longer. The histological appearance of the irradiated kidney in this dog differed from that of the rest of the series, there being scattered glomerular adhesions to Bowman's capsule. We think that this fact may explain its behaviour, the adhesions being evidence of a previously existing renal lesion, since they did not occur in any of the other dogs studied, to the number of over fifty.

In view of the fact that the size of the treated kidney determines to a great extent the amount of damage it sustains, it would naturally be expected that the variations in size in this series depending on the presence or absence of hypertrophy associated with the early or late removal of the sound kidney, would influence the course of the disease. It would also be expected when the irradiation follows nephrectomy that the earlier the nephrectomy is carried out, the greater should be the chronicity of the disease. We consider that the reasons why these expectations are not fulfilled are as follows.

With the good kidney left *in situ*, conditions are ideal for the rapid progress of the lesion in the

treated kidney, which steadily loses its structure, function and reserve power till the thirty to forty day period is reached, when it becomes no longer capable of supporting life by itself. The earlier the nephrectomy is carried out, the less the existing renal damage and the greater the reserve power and the kidney is able to support life for a greater or less period of time after nephrectomy, but always terminating in the thirty to forty day period. Death will not occur before this period, because with the good kidney left *in situ* and disorganization in the damaged kidney therefore proceeding at its maximum rate, this latter can still support life up to the stage mentioned. Life will not be prolonged after this period, as the massive dose of X rays used causes progressive and inevitable renal disorganization, which advances at a definite rate irrespective of all outside factors, and is not affected even when the good kidney is removed and all the reserve power of the irradiated kidney, whether greater or less according to the period of nephrectomy, is brought into play.

When nephrectomy is carried out prior to irradiation, compensatory hypertrophy of the kidney destined for treatment takes place; its size becomes greater and its function increases. The point of importance, however, is that its reserve power becomes less, being partially used up by the hypertrophy it undergoes, so that it follows that the greater the hypertrophy, the less is the reserve power. We have seen already that the greater the size of the kidney, the less the renal damage sustaind by exposure to X rays, so that as the kidney enlarges, its increased size renders it less susceptible to damage, but its diminished reserve power makes it more susceptible. These two components, the diminution in potential damage and the diminution in reserve power, apparently balance one another throughout all stages of the compensatory hypertrophy, and the resultant, the actual damage sustained, remains constant, whatever be the stage at which the X rays are administered, whether before nephrectomy, when there is no hypertrophy, or long after nephrectomy, when full compensatory hypertrophy has taken place, death occurring in the thirty to forty day period in each case.

From our moderately large series we conclude that in any number of full grown normal dogs below ten kilograms in weight, at least 90% will die from renal insufficiency in the absence of complications from thirty to forty days after application of the treatment, provided that opposite nephrectomy has been carried out at any stage prior to this critical period, either before or after the application of X rays.

The Type of the Renal Lesion.

Many of the pathological findings together with the distinct hypercholesterolæmia would seem to classify this type of renal damage by X rays as a lipoid nephrosis. But the slight degree of œdema as well as the polyuria, occasional low albumin content and urea retention indicate rather the existence of a chronic interstitial nephritis, a type which developes later on in the presence of a good kidney. The glomerular changes observed immediately after irradiation may provide the hypothetical inflammation necessary for the classification of the early lesion as a nephritis, but we are not dogmatic on the subject. In this connexion it may be mentioned that some observers, notably Aschoff, hold that degenerative changes, classified as a pure nephrosis, do not occur unless preceded by an inflammatory condition. Further, it is generally recognized that a lipoid nephrosis may be complicated at any time by an interstitial nephritis. Basing our opinions on the previous histological study and on our own functional observations, we consider that the following sequence of events takes place in the experimental lesion: (i) A transient acute nephritis of very short duration occurs; (ii) a period of latency follows; (iii) next a nephrosis of partly lipoid character occurs, supported principally by the extensive tubular changes without glomerular damage, the hypercholesterolæmia, and the presence of doubly refracting bodies in the renal parenchyma and the urine; (iv) this change is followed and complicated by interstitial change which progresses if the good kidney be left *in situ* to a chronic interstitial nephritis.

Modification of the Lesion in Dogs of Larger Size.

The three animals of Group A2 which died in the forty to fifty day period follow consecutively on the first two groups already discussed. Their body weight was from 10·0 to 12·7 kilograms and in each the corerspondingly larger kidney sustained less damage from the irradiation and was able to support life for a longer period. The period of survival, moreover, varied directly with the body weight, though with a larger series of animals we could not be confident of obtaining the same consistent variation. We would, however, venture to forecast in animals of this body weight (10·0 to 12·7 kilograms) a fairly uniform period of survival of forty to fifty days.

In larger dogs the period of survival increases still further. Dog B6, weighing 16·4 kilograms, survived for 131 days. Histological examination of the treated kidney revealed two distinct elements, a completely disorganized and fibrosed area in the middle third of the kidney, which would suffer most from the irradiation, and hypertrophic but otherwise normal renal tissue at both poles, sufficient in extent to support life for this long period. This is well shown in Figure III. Dog A8, weighing twenty kilograms, did not sustain sufficient renal damage to cause death and was killed at 187 days, being at this stage in excellent condition with only slightly impaired renal function. There were large numbers of hypertrophic tubules and normal glomeruli, with only small wedges of fibrous tissue.

Late Changes in the Kidney when its Fellow has been Left in Situ.

As pointed out above, the experiments on the animals whose sound kidney is not removed for a

considerable period, show that after a certain period of time (forty days in average dogs, a longer period in dogs of larger size), the treated kidney is unable by itself to support life. Disorganization of the kidney, either by tubular degeneration or at a later stage by sclerosis, is complete and death occurs invariably within four days. The effect is almost the same as if bilateral nephrectomy were carried out, as practically the whole of the functioning renal tissue is ablated when the good kidney is removed. The glomeruli alone are fairly well preserved and apparently still having some function, though by itself this functional activity is quite inadequate without tubular function, as is shown by the fact that even after seventy-five days in one animal, Dog A15, there was still some secretion from the irradiated kidney.

From the physiological point of view it is of interest to note that the urea concentration of the urine secreted by this atubular kidney was over 2%.

A comparison between the weight of each of the two kidneys at this late stage will be sufficient in itself to prove the impossibility of the treated kidney having any material effect in prolonging life after nephrectomy on the opposite side. This will be apparent also on reference to Figure III.

The Question of Œdema.

The ætiology of renal œdema is far from being understood. The question whether the kidney is or is not the primary cause is still under discussion. Our experiments may have some bearing on this question, because unquestionably in our experimental disease the primary lesion is in the kidney. As shown in the description of our experiments we obtained some œdema, as was shown by the following observations.

1. Puffiness was noted clinically in the face, genitals and limbs and difficulty was frequently encountered in obtaining blood from the saphenous vein for examination, this being obscured by the swelling of the tissues, whereas previously it had been punctured with ease.

2. This puffiness was frequently associated with a slight temporary gain in weight, even though the dog was steadily wasting.

3. There was much water retention, the difference between the twenty-four hour fluid intake and urine output being as high as one litre, whereas normally it is in the neighbourhood of one hundred to two hundred cubic centimetres, as we observed under the same experimental conditions, when normal dogs were used (see Figure IV).

Moreover, this œdema was not of the cardiac type being most commonly observed round the eyes and *post mortem* examination revealed in every animal the complete absence of any cardiac dilatation.

The œdema, further, is unlikely to be due to anæmia, as the fall in the hæmoglobin value of the blood in the great majority of the dogs is not great enough for it to be explained on this ground. On the contrary the latter is possibly more apparent than real in many instances, as the lowered hæmoglobin value may easily be accounted for by hydræmia, which occurred in the experimental disease produced by Allen, Scharf and Lundin.[2] We made no attempt, however, to study changes in the plasma volume.

On the other hand we should emphasize the fact that the œdema is not massive, as seen in certain types of human renal disease. This might be explained by the fact that the lesion we produced is not a clear-cut reproduction of any clinical syndrome, but rather a composite picture into which the elements of a nephrosis of lipoid character and chronic interstitial nephritis both enter. Further it is well known that dogs do not develope renal œdema readily, as compared with human beings and numerous attempts to produce it experimentally have failed,[2] though on the other hand massive cardiac œdema in the dog is easily produced.

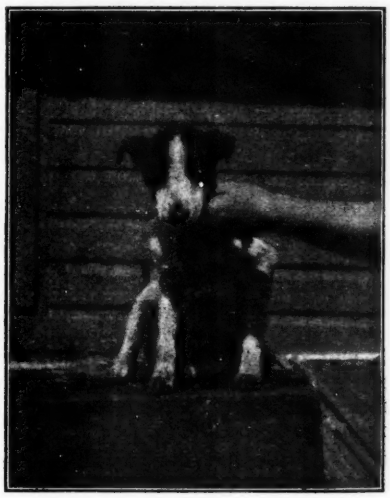

FIGURE IV.

In short, œdema was definitely present in our series of animals and could be accounted for only by the renal lesion. Its comparatively limited extent is possibly accounted for by the fact that dogs do not readily get renal œdema, the fact that our experimental lesion does not reproduce any of the syndromes seen clinically which are accompanied by massive œdema, or both factors combined.

Our observations would appear to support the theory that œdema may occur as the result of a primary renal lesion, though, of course, we have no evidence to discount the theory that a primary tissue œdema may occur with a secondary renal lesion.

The Question of Hypercholesterolæmia and Lipoidosis.

Munk[12] considered that hypercholesterolæmia *plus* lipoidosis of renal epithelium *plus* excretion of anisotropic lipoids is due to a general disturbance of physicochemical nature in the body lipoids. In

our experiments we consider the damage to the kidney as primary and such symptoms as hypercholesterolæmia as secondary to the kidney damage. We also consider the X radiation as the primary factor in the lipoidosis in the kidney. This action of X rays is not typical for kidney epithelium, for apparently similar fatty degeneration has been observed after irradiation of heart muscle,[13] though in this case no examination was made for anisotropic bodies.

According to the recent work of Roffo and Correa,[14] X rays reduce the amount of cholesterol in the blood. This would contradict the observations we made, if we assumed that the hypercholesterolæmia we obtained is directly due to X rays. We therefore conclude that the hypercholesterolæmia is the result of the renal damage, which overshadows the effect X rays have in the opposite direction. The degree of hypercholesterolæmia we observed, though well marked, is not as high as that seen in many cases of human lipoid nephrosis; for example in Group A1 the values are about twice as great as before nephrectomy, while in the human being values much greater still are frequently encountered. A possible explanation of this is the influence of the X radiation in reducing the cholesterol content of the blood, as well as the fact that we have stressed previously that the disease we produced is not an entity, but the result of a composite lesion.

It is interesting to note that the findings observed by us in the kidney, blood and urine form a syndrome which is more or less a reversal of what is believed to take place clinically; instead of having a lipoid nephrosis produced by faulty metabolic processes, we have obtained a clinical and functional syndrome resembling it in many respects, starting from a renal lesion of known ætiology.

We admit finally that the period of observation in these animals has been rather short, as most of them died at a fairly early stage from renal insufficiency; in some who survived for long periods (A8, B6) no attention was paid to this aspect. More information should be gained from a study of the group of animals which received half the usual amount of X rays, the majority of whom survived for several months; this has yet to be reported on.

COMPARISON OF PRESENT STUDY WITH PREVIOUS WORK.

As mentioned above, only one group of investigators has made functional studies in the course of experimental renal disease produced by X rays, namely Hartmann, Bolliger and Doub.[4] These workers made use of a different technique and applied much harder rays than those employed in our investigation through the abdominal wall in fractional doses either to both kidneys or to one kidney after nephrectomy on the opposite side. The number of applications varied in different dogs, the treatment being usually repeated until the experimental lesion was obtained. No attempt was made to correlate the body weight of the dogs with the renal lesion obtained and standardization either of the technique or of the experimental disease was not aimed at.

The late interstitial changes in the lesion were the most emphasized feature of the work, while fatty degeneration and necrosis were apparently not obtained. Stress was laid on the vascular and glomerular changes, which were not a feature in our series. Functional studies differed from our own in the inclusion of phosphate, calcium, iodine and thiosulphate determinations and the extensive use of the phenolsulphonephthalein test, while Andrewes's test was not carried out. The studies, moreover, were over a much longer period of time, due to the greater chronicity of the disease as compared with that obtained by us, which in the majority of cases terminated within the forty day period.

Emphasis, in addition, was laid on the progressive nature of the disease, while the lesion produced by us was one of comparatively short duration, culminating in death from uræmia or followed by repair, according to the body weight.

The series showed a terminal condition of uræmia differing from our own in the absence of œdema and hypercholesterolæmia. Moreover, in many animals the terminal uræmia was apparently precipitated by the last of a series of X ray applications given shortly before, while in our series it was the culmination of a progressive lesion initiated several weeks previously by one application.

To sum up, the lesion in question was a different lesion from our own histologically, produced by a different technique, with also a different clinical and biological termination and therefore not analogous to our own. The object was the production of a chronic interstitial nephritis similar to that seen in man, while ours has been the production of constant lesion of fairly definite duration by means of a standardized technique.

SIGNIFICANCE OF THE EXPERIMENTS.

As mentioned in the introduction to this article, a standardized renal lesion of fairly constant intensity and duration, had not been produced previous to our experiments. We have been able to attain this end by means of a comparatively simple technique. The uses to which such a lesion may be put, are various, in spite of the fact which we have already pointed out, that it does not correspond exactly with any clinical or pathological entity encountered in practice.

First, with regard to therapeusis, the advantages of having a standardized experimental disease easily available for the purpose of therapeutic attempts will be obvious and the question of whether any line of treatment is likely to be beneficial, deleterious or without definite effect on the course of the disease would be decided by its progress in the laboratory animal. A longer period of survival than expected would indicate some possible benefit, a shorter period would discount the value of the treatment exhibited as a possible therapeutic measure.

In the same way information may be gained as to whether the use of any drugs whose full action on the human organism has not yet been fully worked out, may be contraindicated in the presence of a renal lesion. An example of this occurred in the course of our present investigation, when for the purpose of estimating any possible deleterious effect, the anæsthetic "Avertin" was administered several times to a dog suffering from advanced renal disease, during the course of which several aspects of the blood chemistry were studied.[15]

Furthermore, the exact value of any test newly devised or already well known for renal insufficiency can be readily and quickly estimated by comparing the information given by it with the results obtained by other methods during the course of the experimental disease. This is being done by us in the case of Andrewes's reaction on which a report will shortly follow. For these reasons we are of opinion that the disease we have produced has more than a merely academic value.

CONCLUSIONS.

1. A renal lesion of fairly constant intensity culminating in death within forty days from renal insufficiency, provided that the opposite kidney has been removed, has been consistently produced in dogs of medium size by a simple technique.

2. In the latter part of the disease urea retention, acidosis and hypercholesterolæmia occur.

3. The lesion obtained is a nephrosis of a lipoid type preceded by a transient acute nephritis and merging, if circumstances allow, into a chronic interstitial nephritis.

4. In the course of the disease definite œdema, with no apparent basis other than the renal lesion, was frequently observed.

5. In dogs of larger size the renal damage was less and the expectation of life was prolonged for various periods, varying with the weight of the dog.

6. The standardized disease produced in dogs of medium size may be used for the purpose of any research on the diagnostic, metabolic or therapeutic aspect of nephritis.

ACKNOWLEDGEMENTS.

We should like to express our sincere thanks to Dr. M. Cronin, Chief Resident Radiographer of the Royal Prince Alfred Hospital, who was responsible for the whole of the X ray treatment, without whose willing cooperation this work could not have been carried out; to Professor Brown, of the Department of Geology of the University of Sydney, for his assistance and for the use of his polarizing microscope and to the staff of the Departments of Biochemistry and Pathology of the hospital for the unfailing assistance they have given us.

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THE RELATIVE LIABILITY OF AUSTRALIANS, BRITISH-BORN AND FOREIGNERS TO SHOW TUBERCULOUS LESIONS IN AUSTRALIA.

By J. BURTON CLELAND, M.D.,

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IT has been the custom for some years at the Adelaide Hospital, when a thorough and searching *post mortem* examination has been made, to record on special cards the presence or absence of any tuberculous lesion together with the sex and age of the patient, the patient's nationality and if not Australian-born the duration of residence in Australia. If a tuberculous lesion is present, its site and extent are entered and also whether it is active, latent or healed (for example, calcified specks in bronchial glands).

I have already recorded the distribution and other details of tuberculous lesions in eight hundred autopsies performed in Adelaide.[1] Recently the data on five hundred further *post mortem* examinations at the Adelaide Hospital and the Parkside Mental Hospital have been subjected to analysis. Amongst these information as to the birthplace of the patient has been inserted in 383. These were all Adelaide Hospital patients, the birthplaces of the mental patients not having been obtained.

The following tables have been prepared, showing the nationalities of the patients and the prevalence or absence of tuberculous lesions in them. In the case of the Australian-born, we may assume in general that his infection has been contracted in Australia, as war-contracted tuberculosis would be treated almost entirely elsewhere than at the Adelaide Hospital. The British-born[1] comprise English, Scotch and Irish and one New Zealander. The foreigners are very varied, including Americans, Italians, Norwegians, Indians and others. The duration of residence in Australia of the British-born and foreigners varies from two weeks to seventy-six years. Many had been here most of a long life; others died shortly after their arrival, but not necessarily from tuberculosis.

TABLE I.

Place of Birth.	No Tuberculosis.	Tuberculosis.		Total.
		Healed.	Active.	
Australia	131	44	57	232
Great Britain and Ireland (including one in New Zealand)	55	24	19	98
Other Countries	16	4	5	25
Unknown	19	6	3	28
ALL PLACES	221	78	84	383

TABLE II.

Place of Birth.	Number.	No Tuberculosis.	Tuberculosis.	
			Healed.	Active.
Australia	232	56·4%	18·9%	24·5%
Great Britain and Ireland (including one in New Zealand)	98	56%	24·4%	19·4%
Foreign Countries	25	64%	16%	20%
Unknown	28	67·8%	21·4%	10·7%
Great Britain, Ireland, and Foreign Countries	123	57·7%	22·7%	19·6%

Though the figures are small, it would seem as though the Australian does not enjoy any more definite lessened liability to tuberculosis than the British-born. Amongst the Australians 56·4% had no sign of any tuberculous lesion, amongst the British 56% and amongst the few foreigners 64%; British-born and foreign-born added together gave 57·7%. It may seem from the tables as though the British-born, having contracted a tuberculous lesion, was more likely to overcome it than an Australian and that conversely in the Australian the tuberculous lesion was more likely to be progressive and to cause death. The figures are too small, however, to stress this aspect. Moreover, another explanation may be suggested. The small tuberculous foci that undergo healing and calcify, are probably frequently contracted in childhood. In the case of a British-born or foreign-born person, if the lesion did not heal, but was progressive, the individual would not be likely to emigrate to Australia or attempting to do so, would not be likely to be admitted. Thus there may be some tendency for those persons coming to Australia from abroad to have a higher percentage of healed tuberculous lesions amongst them when compared with the Australian born, being in fact to some extent selected from the point of view of tuberculosis.

[1] The term "British born" is used here for convenience to mean born in Great Britain or Ireland.

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THE NON-OPERATIVE TREATMENT OF CERVICITIS.

By R. FRANCIS MATTERS, M.D., F.R.C.S. (Edinburgh),
Lecturer in Human Physiology, University of Adelaide; Tutor in Obstetrics, Queen's Home; Surgeon to the Night Clinic for Female Patients, Adelaide Hospital.

As the orthodox text book treatment of cervicitis is usually operative, an account of non-operative treatment given adequate personal trial might be of interest and value.

It is to Cumberbatch and Robinson, of Saint Bartholomew's Hospital, that I am indebted for training in the methods which are first described, and the measure of success that has accrued to me in the diathermy treatment of gonococcal cervicitis warrants a report upon the same.

Exposure of the cervix is obtained with a bivalve speculum, light being reflected by means of a head mirror. The cervix and vagina are cleaned with a weak solution of *liquor potassæ*. The endocervix is next swabbed with tincture of iodine, after which a hollow, active electrode is fitted into the cervical canal so that about 3·8 centimetres (one and a half inches) actually enter. The inactive electrode may be a metal belt which encircles the body at the level of the umbilicus. When all is ready, the current is turned on and by means of a thermometer in the cervical electrode the temperature may be gradually raised to 46·6° C. (116° F.), at which temperature the endocervix is maintained for fifteen minutes. After this the endocervix and *portio vaginæ* are painted with 15% mercurochrome 220.

In addition to the foregoing a 3% solution of mercurochrome is injected into the subendocervical tissues in several points of the periphery in the manner originally suggested by Gellhom and later by Kelvestine and Farmer.

Following this a glycerin tampon is placed in the vagina and the speculum removed.

The diathermy is repeated every third day, while the mercurochrome injections should have two weeks as an interval. The results have been most gratifying, especially in a disease that has been therapeutically recondite for so long.

Non-Specific Cervical Affections.

Non-specific cervical affections may be either frank pseudo-adenomata or lesions due to *post partum* cervical lacerations. In the former condition fairly good results are obtained from diathermy together with the infiltration with mercurochrome and cervical swabbing. Much better results, however, have been obtained from the use of the cautery. Ionization with copper and zinc ions did not give the results which were originally anticipated, so far as our patients were concerned.

The cautery method was first explained to me by Matthews, of the Long Island College Hospital, New York. The technique is as in diathermy treatment until the active electrode should be inserted. At this point a cautery is used and the large red cervix is cauterized in strips, these being made radially and extending to a depth of six millimetres (0·25 inch). The patient subsequently douches daily with a saline douche. When the cauterized strips heal, the adenomatous tissue is contracted and covered with squamous epithelium.

When the cautery is first applied, the cervical canal itself may require attention and any *ovulæ Nabothi* destroyed at the same time. Where there are lacerations it is better to cauterize the opposite sides of the fissure and these eventually fold in and cover the lacerated surface.

In a very limited number of instances radium needles have been inserted into the cervical tissue if a possibility exists that early carcinoma might have commenced. These patients have responded most remarkably and large bulky cervices have very considerably reduced in size. Fellow surgeons to whom the radium needles have been hired, have supported these observations.

The two latter methods are superior to cervical amputation in subjects at the child-bearing age, since that operation is sometimes followed by abortion or even rupture of the lower uterine segment during labour.

Reports of Cases.

WIDE PROPAGATION OF A CARDIAC MURMUR.

By GUY GRIFFITHS, M.D. (Sydney),
Senior Honorary Physician, Royal North Shore Hospital of Sydney.

E.M.T., a female, aged eighteen, was admitted to the Royal North Shore Hospital of Sydney on February 18, 1929, for a minor surgical operation.[1] As the honorary surgeon was alarmed at the loudness of her cardiac murmurs, he asked me to see her and to advise if she were suitable for an anæsthetic. On auscultating her precordium, I recognized an astounding murmur that I had heard nearly twelve years previously, and I subsequently recognized the patient who told me that she had been in the hospital under my care in 1917. In that year she was demonstrated at a meeting of the New South Wales Branch of the British Medical Association in the building in Elizabeth Street, and her condition is described in THE MEDICAL JOURNAL OF AUSTRALIA for July 7, 1917, under the title of "Wide Propagation of a Cardiac Murmur." She has a systolic murmur which is loudest over the apex of the heart about ten centimetres (four inches) from the middle line and can be heard all over the chest back and front and even in the loin. One or two physicians armed with phonendoscopes succeeded in hearing it even on the top of the head. Once it has been heard in the chest, it is easily picked up in the femoral canal. Nevertheless, she is bright, active, of good colour and fit for ordinary work. She has no œdema and no cyanosis, in fact no evidence of cardiac disease excepting only the murmur and very slight dyspnœa on severe exertion.

When she left the hospital in 1917, she was running about bright and well and she tells me that she has continued so ever since, except for the recent slight surgical affection and for an attack of measles about 1919. There has been no recurrence of the rheumatic fever.

The description of her condition in THE MEDICAL JOURNAL OF AUSTRALIA in 1917 attracted the attention of Dr. J. Heitz, of Paris, who asked permission to reprint it in *Les Archives des Maladies du Cœur, des Vaisseaux et du Sang.*

It has been suggested that this is a case of coarctation or stenosis of the aorta. As, however, the murmur was not heard on the little patient's first admission when six years of age—and so loud a murmur could scarcely have been overlooked—but arose only when the heart was widely dilated during the course of a bout of rheumatic fever, it appears certain that the rheumatism was causal. How it is propagated to so great a distance I do not know.

[1] The patient was demonstrated at a clinical meeting of the New South Wales Branch of the British Medical Association on June 13, 1929.

Reviews.

INJECTION TREATMENT OF VARICOSE VEINS.

"VARICOSE VEINS," by H. O. McPheeters, is a book which is well bound, well printed, well illustrated and badly written.[1] In this respect it is unique. It is almost unbelievable that in these modern days of publication a book would be published containing so many glaring errors. These are not mere slips, but occur on almost every page. Hybrid phrases, "ulcer cruris," "saphenous magna," are common. Names are spelt incorrectly, for example, "Reynaud's disease," "pampinaform plexus." Spelling is not uniform. On page 30 "dilation" and "dilatation" occur on consecutive lines. These, however, are the least of the author's sins. The adjectives used throughout the book are amazing, for example, "inner thigh," "cadaver speciman," "varicosed vein," "fleshy women" *et cetera* and do duty with almost monotonous regularity for adverbs. "Secondary" and "post-operative" occur throughout as adverbs. An example on page 29, "which were watched to as high as 86 days post-operative," is a gem. Many sentences are scarcely intelligible, for example, "they (the valves) are just back of and supporting the column of blood" (page 25).

There is no doubt that the author has carried out quite a considerable amount of investigation. He has investigated the direction of flow in veins by the injection of solutions impervious to X rays and repeated the experiments of Sicard and Jentzer, although he makes no reference to their work. He has also investigated the histological changes which take place in varicose veins following the injection of sclerosing solutions. In the text reference is made to various tests, for example, page 45, positive Trendelenburg, Trendelenburg double and von Perthes's modification, but no attempt is made in the book to explain these tests.

A chapter has been included on elephantiasis, though what exactly this has to do with varicose veins is not explained; it is merely in keeping with the general jumble.

Much of the advice given is of dubious value and the book is not recommended.

[1] "Varicose Veins, with Special Reference to the Injection Treatment," by H. O. McPheeters, M.D., F.A.C.S.; 1929. Philadelphia: F. A. Davis Company. Demy 8vo., pp. 208, with illustrations. Price: $3.50 net.

BACTERIOLOGY.

THE extensive additions to our knowledge of bacteriology during the past three years have made necessary the publication of a new (ninth) edition of Park, Williams and Krumwiede's "Pathogenic Microorganisms."[1] This will be found of value to all laboratory workers dealing with medical bacteriology and protozoology.

Part I is devoted to the general characteristics and methods of study of all the microorganisms (vegetable and animal) which are considered. The classification has been rearranged in order to conform to the classification of the American Society of Bacteriologists. There is included a table for identification of bacteria and spirochætes and this includes both the common terminology of the organism and that recommended by the American Society of Bacteriologists. In the present transition stage of classification this table is of distinct value.

More attention could be devoted to the chapter on procuring and handling of material for examination. If this were better understood by the practitioner, better results would be available from the laboratory. The difference between surgical asepsis and bacteriological sterility is not always understood.

Toxins and antitoxins and antimicrobial or antiprotein substances receive adequate treatment and in the chapter on complement fixation tests there are included detailed accounts of the Kahn, Kline and Meinicke tests for syphilis. There is a brief discussion of the bacteriophage phenomenon.

In Part II the microorganisms secure individual consideration. The descriptions are detailed and well illustrated while not overloaded. In the previous edition the practical application of sera and vaccines was collected together into Part III of the publication. In this edition this information is presented under each individual organism and should be a decided improvement.

The chapter on the pyogenic cocci, pneumococci and paratyphoid bacilli have been practically rewritten and advances in our knowledge of scarlet fever, measles, yellow fever, undulant fever, tularæmia *et cetera* are described.

There is a description of the results of the feeding of Calmette vaccine to infants for the prophylaxis of tuberculosis. Pathogenic moulds and yeasts, filterable viruses and protozoa have been well described.

Part III deals with the bacteriological examination of water, air, soil, milk and shell fish. The detailed technique is given.

The book concludes with a description of the standardization of disinfectants and the methods of disinfection. As noted in the preface, the book is not intended for medical students—the student will be suited by a much less detailed account of the subject; but if this book adorned the shelf of every medical practitioner and was read by him, it would be a distinct service to bacteriologists.

PHARMACOLOGY.

THE "Extra Pharmacopœia" of Martindale and Westcott has deservedly so wide a reputation that it has reached its nineteenth edition and the second volume of that edition is now to hand.[2] The first volume, issued in June, 1928, is devoted mainly to treatment by drugs. The second volume deals with matters of diagnosis, analysis and assay of *materia medica* and many other topics, such as animal organotherapy, physiological standardization, determination of hydrogen ion concentration of solutions, scheme for the recognition of organic substances used in therapeutics, iontophoresis, radiology, ultra-violet rays, radium, uranium and uranium "X," methods for examining urine, blood, fæces, cerebro-spinal fluid and pleural and peritoneal fluids, analysis of water, milk and butter, margarine, gas poisoning, food preservatives, ptomaines, embalming, bacteriological and clinical notes and very many other subjects. The amount of information contained in these volumes is enormous and is brought thoroughly up to date. Every practitioner should obtain both volumes of the successive editions of this work. It is the policy of the editor to publish the second volume after complete revision a year later than the first. In the present volume the authors note the possible injurious effects of peroxides and aldehydes as impurities of ether. The assay of digitalis leaves is carefully considered and it is stated that the Ouabain process, as used in the United States, is unsound. The Pharmacological Laboratory of the Pharmaceutical Society of Great Britain holds that not one ounce of the liquid extract of ergot of the British Pharmacopœia of 1914 can be of the slightest medicinal value. Iodine deficiency in natural waters, vegetables and animal foods and its relationship to goitre are critically considered. The chapter on vitamins is brought completely up to date and useful information is given about flour bleaching and "improvers." An excellent summary of the controversy as to the relative merits of wholemeal and white bread makes very interesting reading. Of cod liver oil the vitamin content is in the following order: Scotch, Newfoundland, Norwegian. It is stated that the opium poppy grown in England does not elaborate morphine. The renal function tests are described with concise instructions. In the bacteriological notes the method of carrying out the Schick test is given. "It is hoped the use of toxoid instead of toxin-antitoxin mixture will prevent recurrence of fatalities." The relationship between acute poliomyelitis, cerebro-spinal fever and *encephalitis lethargica* is dwelt upon. Reference is also made to post-vaccinal encephalitis. The employment of serum to achieve passive immunity in measles is considered, as are also the Dick test and the Schultz-Charlton blanching test for scarlet fever. The intramuscular injection of convalescent serum for poliomyelitis is held to be of distinct value. It is further stated that Haffkine's vaccine for plague has saved several millions of lives. It is impossible in a review to cover the whole of the ground of this most comprehensive work. It is full of the most valuable information for the practising physician and surgeon, the pharmacologist, the public health official, the pathologist and bacteriologist and the votaries of other branches of the healing art. A minor misprint occurs where *Eucalyptus nemiphloia* should read *hemiphloia*. Otherwise the article on eucalyptus oil is excellent.

[1] "Pathogenic Microorganisms: A Practical Manual for Students, Physicians and Health Officers," by W. H. Park, M.D., A. W. Williams, M.D., and C. Krumwiede, M.D.; Ninth Edition, Enlarged and thoroughly Revised; 1929. Philadelphia: Lea and Febiger; Royal 8vo., pp. 819, with illustrations. Price: $6.50 net.

[2] "The Extra Pharmacopœia of Martindale and Westcott," Revised by W. Harrison Martindale, Ph.D., Ph.Ch., F.C.S.P. Nineteenth Edition; Volume II; 1929. London: H. K. Lewis and Company, Limited. Foolscap 8vo., pp. 792. Price: 22s. 6d. net.

A MANUAL FOR THE DIABETIC PATIENT.

THE fact that the diabetic patient needs instruction in the scheme of his treatment has led to the production of "The Diabetic A B C," a practical book for patients and nurses, by Dr. R. L. Lawrence, so well known for his writings on diabetes and his line diets.[1] The book is written in simple language, easily understandable and is specifically designed to help the diabetic to play his part in the scheme of his treatment. Naturally the dietary instructions are mainly based on the use of the line rations and several pages are devoted to showing how to get ample variety of foods and meats with many tasteful recipes, all based on the line rations. In addition the so-called five gramme scheme of dieting is illustrated in which the diet is worked up by first calculating the carbohydrate and then building up the necessary protein and finally the fat—in our opinion a much more satisfactory and more elastic method of dieting. Full instruction is given in the method of using "Insulin" and in its dangers and in what is to be done if overdosage should occur. A short chapter on urine testing is added and one on "extras of no food value" and on "drinks for diabetics" complete a very useful little manual which can be confidently recommended to these sufferers.

[1] "The Diabetic A B C," by R. D. Lawrence, M.A., M.D., M.R.C.P. (London); 1929. London: H. K. Lewis & Co., Ltd. Demy 8vo., pp. 55. Price: 3s. 6d. net.

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SATURDAY, MARCH 15, 1930.

Medical Ethics.

THE distinction between right and wrong, between moral and immoral behaviour, between responsibility and dereliction of duty is dictated by convention. Apart from religious teaching, men devise customs and laws according to the conditions of life of the race or age to render social intercourse safe and advantageous. A wild animal has but one law to govern its behaviour: the law of its own protection. Since man endeavours to emancipate himself from the savage beast of the jungle, he instinctively sets up two theses, that human life is sacred and may not be destroyed and that the law of possession must be respected. No one has any difficulty in understanding that ethical conduct connotes obedience to a code of morals and the adequate performance of duties. The law and custom define morals and duties.

Medical ethics do not differ in their essence from social ethics. They are based on the desirability to hold human life and human health sacred and on the principle that the law of possession must be held inviolate. The legal code has become complicated and involved, because man realizes that the fundamental principles on which ethics are founded, can be applied in countless ways and adapted to an endless variety of circumstances. In the same way medical ethics have been extended and increased in order that the essential principles may be applied to the conduct of a medical practitioner's whole professional existence. Each rule of medical ethics has been devised as the result of experience and with the definite purpose of safeguarding the health, lives and belongings of the community. When a patient entrusts precious secrets to his doctor, the latter has to recognize that the information is the patient's property and must be protected. It is strange that although the non-medical person understands what is meant by ethics, he is profoundly ignorant concerning the significance of medical ethics. Some months ago the President of the New South Wales Institute of Journalists in a letter published in this journal manifested the usual confusion between etiquette, the rules of polite behaviour, and ethics. He gave two instances of what the General Medical Council would regard as unethical conduct, if not infamous conduct in a professional respect; the advertising of a medical practitioner's name in connexion with his practice and the advertising of a medical practitioner by the publication of a portrait in a lay newspaper. The General Medical Council has realized that unless both direct and oblique advertising by medical practitioners is strictly prohibited, the whole basis of the proper relations between a doctor and his patient would be destroyed. The lay press or a considerable section of it has little use of accurate statements of medical facts unless they can be published in connexion with the name and portrait of some medical practitioner. Moreover, a medical paragraph has but small news value unless it is clothed in sensational language. A recent instance of the manner in which some newspapers handle a piece of cold scientific information may be quoted. Dr. J. B. Collip, of the Department of Physiology at the University of Toronto, has been working with the cortical substance of the adrenal gland and has isolated a substance which seems to have some power to act as a lytic agent of certain malignant cells. The details of the work must be studied before any opinion can be formed concerning the significance of this work. We understand that the Toronto investigators refrain from making any claims. One newspaper explained to the public in connexion with this new "cure of cancer" that cortex is the outer layer of the brain and the adrenal gland is a small structure situated above the kidney. No doubt the public was duly impressed, even if the medical profession was amused at this quaint interpretation of a badly worded cablegram.

Within the last few years the leaders of the medical profession have been greatly concerned in regard to the attitude of a few members in regard to three or four points in medical ethics. The first is that of advertisements in the lay newspapers.

The Branches of the British Medical Association in Australia have unfortunately sanctioned the insertion of notices of change of address, of resumption of practice after a holiday or illness and of commencement of practice. These advertisements are not permitted in Great Britain. They are quite unnecessary from the patients' point of view and they are often abused by a disregard of the prescribed conditions of the notices. Apart from these sanctioned advertisements, there are those other forms of advertisement to which the medical profession takes such grave exception. These advertisements are often inserted without the knowledge or sanction of the medical practitioner named and often cause him much annoyance. The newspapers have been told times without number that there is a real objection to the publication of information concerning the treatment of a person by a named doctor. When a medical practitioner is called upon to attend anyone, all that transpires between him and the patient is confidential and should not be made public. The fact of the attendance is of no concern to anyone other than the patient. We fail to recognize that these matters have any news value. Moreover, when these parochial announcements are inserted in a newspaper, the medical practitioner is placed in an unenviable position. If he has sanctioned the publication, he runs the risk of having his name removed from the medical register. At times it is extremely difficult to prove that the paragraph has appeared without his knowledge and consent.

The matter of portraits is just as important. In this connexion we note with extreme regret that the Senate of the University of Sydney when announcing the appointment of three Bosch professors, handed to the lay press the portraits of the successful candidates. Could anything be more undesirable than the publication in the lay press of the portraits of those men who by teaching and precept will mould the lives and actions of the next and successive generations of medical practitioners? What answer can be given to the student who asks why he is not permitted to have his portrait in a newspaper when the portraits of his teachers have appeared without protest?

The subject of the splitting of fees must be reserved for another occasion. This immoral act is, unfortunately, still being practised in the Commonwealth.

Current Comment.

THE ACTION OF THE DIAPHRAGM.

Although the importance of the diaphragm in respiration is generally recognized, little thought is given by some to the fact that it has certain functions in connexion with the separation of the œsophagus from the cardiac end of the stomach. Were it not for the diaphragm and the arrangement of muscular tissue at the lower end of the œsophagus man would be continually subjected to what Rupert Brooke described as "acrid return and slimy," with all its unpleasantness. The average clinician takes most of these facts for granted. The diaphragm, however, and its action have been forcibly brought under consideration by the adoption of phrenic avulsion as treatment for certain pulmonary conditions.

Minas Joannides has recently discussed the relationship of the diaphragm to the stomach.[1] Early in 1929 Joannides reported the presence of two different types of contraction in the cardia of the anæsthetized dog. He observed these by inserting his finger into the œsophagus through a gastrostomy opening. One type of contraction, the œsophageal, was circular and constricting. It could be produced by stimulation of the peripheral end of the vagus and also by stimulation of the œsophagus itself at any level above the gastro-œsophageal junction. The second type, due to the contraction of the diaphragmatic pillars, was described by him as a progressively downward milking contraction and was coincident with each inspiration. This diaphragmatic contraction became more pronounced when diaphragmatic breathing became more forcible. Joannides has now made a further series of observations by examining a normal human subject with the fluoroscopic screen after a barium meal had been given. When the barium reached the cardia the subject was asked to breathe deeply. With each inspiration the œsophagus was seen to become constricted at the cardia to such a degree that no barium could be seen below the diaphragm. The œsophagus above this constriction became ballooned. The picture seen was in some respects similar to that seen in so-called cardiospasm. It was also regarded as corresponding with the terminal phase of the downward "milking" contraction previously described by Joannides in the cardia of dogs. The contraction was transitory and with the onset of expiration the diaphragm was noticed to rise and with the occurrence of the relaxation the barium ran freely into the stomach.

[1] *Archives of Internal Medicine*, December, 1929.

Joannides also found that when barium was introduced into the stomach, a large bubble of air was also introduced. He was thus able to study the phenomenon of belching. He refers to the description by Jackson of a "kink of the œsophagus" which normally prevents regurgitation when a man stands on his head. This kink, according to Joannides can be demonstrated by radiography. He found that belching was brought about by the coordinate contraction of the abdominal wall, the stomach and the part of the diaphragm arising from the costal cartilages, while the portion of the diaphragm arising from the vertebræ was relaxed. He thinks that in belching the contractions of the diaphragm push the fundus downwards and in a medial direction and thus release the kink that is formed at the junction of the cardia and the fundus.

In regard to the two types of contraction observed by Joannides in anæsthetized animals subjected to gastrostomy, it would be justifiable on account of the artificial circumstances of the observation to doubt their occurrence in the normal person. Since they have been observed on radiological examination, however, it must be conceded that they occur. At the same time it is doubtful whether they are both necessary to health and comfort. The constricting contraction, as already mentioned, is due to the action of the vagus. The second or "milking" contraction is the direct result of respiratory movements of the diaphragm. Joannides points out that this contraction initiates gastric peristalsis. Because peristalsis follows on this contraction it is not necessarily initiated by the contraction. So far no disability has been reported in a patient who has been subjected to phrenic avulsion. A series of observations such as those made by Joannides with the fluoroscopic screen should be made on such a patient. It may safely be concluded that movements other than those of the diaphragm associated with deglutition can initiate gastric peristalsis. It would also be useful to determine whether it is easier for a person with a paralysed diaphragm to induce belching than for one whose diaphragmatic nerve supply is intact.

No discussion on this part of the body would be complete without reference to the condition known as cardiospasm. According to Joannides Chevalier Jackson has described the term cardiospasm as a misnomer, for he could find no sphincteric muscular arrangement at the cardiac end of the œsophagus. The views on the ætiology of cardiospasm are numerous. For instance Rosenstein holds that the condition is due to atony of the œsophagus with secondary spasm of the cardia. Kraus holds somewhat similar views, but thinks that degenerative changes in the vagi are responsible. Other observers invoke disorders of the neuro-muscular mechanism as an explanation. Disturbance of the inhibitory control exercised by the sympathetic system has been held to be due to either central, reflex or intra-œsophageal causes. Joannides states that the pillars of the diaphragm are separated from the cardia by areolar tissue and that they bear a resemblance to the fibres of the *sphincter ani*. He suggests that cardiospasm may be an exaggeration of the normal contraction of the diaphragmatic pillars. He adds that a persistent spasm of these bundles will cause a chronic obstruction at the cardia. He does not follow this statement with the logical corollary that cardiospasm in these circumstances would be cured by the production of paralysis of the diaphragm. As far as cardiospasm is concerned, the weight of evidence is in favour of some involvement of the sympathetic nervous system. It should be possible to produce spasm of the diaphragm in laboratory animals and, if this were followed by administration of a barium meal, useful information might be gained.

PARADOXICAL EMBOLISM.

THE occurrence of an embolism in the systemic arterial system implies the presence of an original focus either in the left side of the heart, in the great vessels or in the lungs. Embolism may also reach the systemic arteries from the right side of the heart by way of a patent *foramen ovale*. This condition has been known as crossed embolism and as paradoxical embolism, a term used by von Recklinghausen. It is of rare occurrence and it holds not only an anatomical, but also a clinical interest from the point of view of diagnosis. Theodore Thompson and William Evans have recently given a detailed account of five cases, have reviewed the literature and have discussed the mechanism.[1] They divide paradoxical embolism into three distinct types. In all these the embolus travels from the right side of the heart through a persistent *foramen ovale* or a patent interventricular septum. The subdivision is made according to the nature of the embolus, whether it be a simple thrombus, a fragment of new growth or a piece of septic material. Four of their cases fall into the first group and one into the second. The most interesting of the group is that of a woman, aged 38 years, who suffered from phlebitis following appendicectomy. Pulmonary infarction occurred twice and then complete motor aphasia supervened with right hemiparesis. The patient recovered. Thompson and Evans refer to the view that an increase in the blood pressure in the right auricle is necessary before an embolus can pass through a patent *foramen ovale*. Normally the pressure in the left auricle is higher than that in the right and thus a foramen which is anatomically patent, remains competent from a physiological point of view. When pulmonary infarction occurs the right auricular pressure is raised and passage of an embolus through a patent foramen is possible. From the point of view of diagnosis this condition is interesting. It is obvious that most difficulty will be experienced in excluding involvement of the lung in the presence of an embolus composed of malignant tissue and it will always be necessary to consider the possibility of the existence of a dual focus in the venous circulation and in the left side of the heart.

[1] *The Quarterly Journal of Medicine*, January, 1930.

Abstracts from Current Medical Literature.

PHYSIOLOGY.

Vascular Reactions of the Colon to Fright.

A. N. DRURY, E. FLOREY AND M. E. FLOREY (*Journal of Physiology*, October, 1929) made the accidental observation on a dog with a double Thiery fistula of the colon, that the exposed mucous membrane became very pale when the dog was at all alarmed. They have studied the effect of various kinds of stimuli on the vascular reaction of the colonic mucous membrane. Any cause of alarm, such as banging of a table or the approach of a strange person, resulted in a very rapid and extreme pallor of the mucosa. A severe fright, such as that produced by the inhalation of a small quantity of ether for about five seconds, initiated a most intense blanching which lasted ten to fifteen seconds. The dog always exhibited the emotion of fear before the onset of any recognizable vasomotor symptoms. This is opposed to the James-Lange theory of emotions which supposes that a visceral reaction occurs in response to a stimulus and that this reacts on the higher centres producing the quality of the emotion. Persons suffering from "nervous dyspepsia" may be victims of excessive visceral vasomotor reactions, whereby their digestive glands are deprived of a considerable part of their blood supply as a result of the reactions to slight external stimuli.

Duodenal Regurgitation.

W. N. BOLDYREFF who first claimed that regurgitation of duodenal contents into the stomach is an important means of reducing the acidity of the gastric contents towards the end of the period of gastric digestion, has replied to the various attacks that have been made recently on this claim (*Bulletin of the Battle Creek Sanitarium and Hospital Clinic*, October, 1929). He claims that he has established that the pancreatic juice in normal conditions is the only important factor in neutralization of acid inside the stomach. Hyperacidity consists mainly of a decreased neutralization of the acid of the gastric juice in the stomach as compared with the normal and is not due to increased secretion of acid. The causes of this should be sought in the condition of the pancreas. Entrance of the duodenal secretions into the stomach occurs as a purely physiological phenomenon under the following four conditions: (i) When the stomach and the duodenum are empty and the reaction in both is alkaline; (ii) with abundance of any acid in these organs (automatic regulation of acid in the stomach by alkaline pancreatic juice); (iii) with abundance of fat in these organs and (iv) with any strong irritation of the duodenal mucosa (hot and cold liquids, alcohol, caustic substances *et cetera*). The greater part of the regurgitated fluid always consists of pancreatic juice. Under the first and third conditions there is abundant admixture of bile and the pancreatic juice is very rich in all its ferments. Under the second condition the bile is usually absent and the pancreatic juice is poor in ferments, but has a high alkalinity; normally the admixture of intestinal juice is insignificant, but in the presence of an insufficiently functioning or diseased pancreas the intestinal juice reaches the stomach in very large quantities.

The Hormones of the Female Reproductive Cycle.

E. C. DODDS AND F. DICKENS (*The Journal of Obstetrics and Gynæcology of the British Empire*, Spring Number, 1929) have published an account of the problems of reproduction in the human female from the point of view of experimental biology and biochemistry. They deal with the cause of the onset of puberty and the establishment of menstruation and its continuance, the phenomenon of pregnancy including the cessation of menstruation and mammary enlargement and lactation. During the prepuberal period the anterior lobe secretion is used for general growth. With the advent of puberty and the falling off of general growth the secretion is set free for ovarian development. The ovary increases in size and begins to produce the œstrum-producing hormone. This hormone is responsible for the increase in size of the uterus and the mammæ. This is definitely established for lower animals and the macaque whose cycle closely resembles the human cycle, was used for the injection of the œstrum-producing hormone with positive results. The authors discuss ovulation and argue that menstruation can occur in the absence of ovulation and of a *corpus luteum*. The *corpus luteum*, however, is necessary for the sensitization of the uterus in preparation for the growth of the placenta.

Respiratory Response to Physical Training.

E. C. SCHNEIDER AND G. C. RING (*American Journal of Physiology*, December, 1929) have studied the influence of a moderate amount of physical training on respiratory exchange and breathing during physical exercise. They find that moderate physical training, about an hour a day, increases the load-carrying ability within one week, but that the full effect is observed only after five to seven weeks. Any variation in the regularity or reduction in the amount of daily work soon reduces the load-carrying ability, but even with complete neglect of exercise some of the gain in power is maintained for several months. The percentage of carbon dioxide exhaled and of oxygen absorbed during work is increased by training; the full effects are reached within four to five weeks. These soon drop back to the pretraining level when training is discontinued. The minute volume of breathing for any given load of work decreases with training and reaches its lowest level in four to six weeks. The effects of physical training are manifest in the subject sitting at ease by a higher percentage output of carbon dioxide and intake of oxygen and by a higher metabolism per square metre of body surface.

Use of Metabolic Waste Heat in Muscular Exercise.

DAVID RAPPORT (*American Journal of Physiology*, December, 1929) has investigated the utilization of the "waste heat" of metabolism in muscular exercise. The evidence presented indicates that the specific dynamic action of carbohydrate and fat is not necessarily waste energy and that these foods are not only used, but are used economically in muscular exercise. In other words the extra energy from ingested fat and glucose which at rest appears as waste heat, is utilized as free energy in muscular work. On the other hand the calorigenic action of epinephrin and the specific dynamic action of tyrosine, like that of protein, cannot be used in muscular work. The experiments confirm the conception that the calorigenic action of epinephrin is due neither to muscular work nor to the specific dynamic action of carbohydrate.

Milk and Fat Secretion.

NUMEROUS and diverse hypotheses have been advanced to explain the formation and secretion of milk. W. E. Petersen, L. S. Palmer and C. H. Eckles (*American Journal of Physiology*, November, 1929) have studied the mode of synthesis and secretion of milk fat in the cow's udder. One gland was milked at the time of slaughter and the other gland on removal after slaughter. As more or nearly as much milk was secured in the *post mortem* as in the *in vivo* milkings, it is concluded that the cow's udder not only can but does contain practically all the milk produced at a milking. The same fact shows that in all probability the milk is secreted at a more or less constant rate in the interval between milkings. This conclusion is contrary to the general belief that a greater or less portion of the milk drawn at milking is secreted at milking time. The much lower fat content of *post mortem* milking lends support to a hypothesis that milk fat is secreted by a separate mechanism from the one responsible for the secretions of the other ingredients of milk.

The So-Called Heart Hormone.

As a result of the observed effects of extracts of different parts of the heart several authors have suggested that the heart beat is regulated by a "humoral" substance produced chiefly in the sino-auricular node and right auricle. Enid T. Oppenheimer (*American Journal of Physiology*, November, 1929) has investigated more completely the specificity of this

stimulating and activating substance. The results reveal the frequent presence in extracts of heart muscle of a substance which has a stimulating action on the heart, causing augmentation and often acceleration of the beat, but followed often by a toxic action. Similar effects, somewhat less pronounced, are obtained by the use of extracts of other tissues, such as striped and plain muscle, liver and lung. The results do not confirm the theory of a specific heart hormone, but rather support the view of a widely distributed substance occurring in most tissues and possessing in adequate concentration an augmenting action on the heart.

BIOLOGICAL CHEMISTRY.

Variations in the Morning Alkaline Tide of Normal Individuals.

ROGER S. HUBBARD AND T. MURRAY STEELE (*Journal of Biological Chemistry*, October, 1929) have studied the effects of variations in foods upon the reaction of urine secreted by normal subjects after a meal has been taken. They found that all subjects do not respond in a similar way in such experiments. In some subjects the changes in reaction were found to correspond closely to those which would be expected if the gastric secretion induced by foods caused a relative alkalosis in the body and a subsequent alkalinity of the urine, for when food is omitted, the changes do not occur. In others an increased alkalinity of the urine developes, whether food is taken or not. In these there seems to be an acid-alkali rhythm which does not depend on the immediate stimulation of the gastric glands, but which may be secondary to a secretory rhythm of the stomach. In another group of subjects the workers found a definite alkalinity developing before any meal is eaten and this might persist throughout the entire morning period, even when no food was taken.

The Effect of an Exclusive Meat Diet on the Blood.

EDWARD TOLSTOI (*The Journal of Biological Chemistry*, September, 1929) has investigated the effect of an exclusive meat diet on the blood. He collected specimens of blood before the meat diet was instituted and at monthly intervals thereafter and also at the close of the experiment. The possibility of renal damage suggested the study of some of the non-protein nitrogenous constituents and the traditional association of meat with uric acid made the study of this substance desirable. As the plasma manifested a milkiness soon after the beginning of the experiment, the blood cholesterol was observed. Only a few analyses of the calcium and phosphorus were made. The carbon dioxide combining power of the blood was determined because of the ketonuria and its probable effect on the alkali reserve. Analyses of sugar, plasma proteins and chlorides were also included. The methods used for the various analyses are mentioned. The author found that the chemical composition of the blood was little affected by such a diet, except for a lipæmia and hypercholesterolæmia which in one subject reached a maximum of 800 milligrammes per hundred cubic centimetres on one occasion. This increase did not persist after the meat diet was discontinued and is attributed to the large quantity of ingested fat. A visible lipæmia was present in all specimens. The uric acid content rose and after about three months fell, although the diet was continued for five months after the elevation had been noted. The carbon dioxide combining power of the blood remained within normal limits in spite of the daily ketonuria over the entire period of the experiment. There were no changes in the constituents of the blood that might suggest that renal damage had occurred.

The Reaction of Alkaline Urine.

R. S. HUBBARD (*Journal of Biological Chemistry*, October, 1929) has made a study to explain the changes in the reaction of the morning urine. There are two factors which must be taken into consideration. One is the secretion of hydrochloric acid by the stomach which causes alkalinity after a meal is taken. The other is probably an adjustment of the respiration to waking conditions which frequently shows its effect very early in the morning. The author concludes that if the interplay of these two factors is kept in mind, most results can be understood.

The Status of the Therapeutics of Irradiated Ergosterol.

ALFRED F. HESS, J. M. LEWIS AND HELEN RIVKIN (*Journal of the American Medical Association*, August 31, 1929) describe the status of the therapeutics of irradiated ergosterol. They found normal concentrations of inorganic phosphorus and calcium in the blood in rickets due to lack of an antirhachitic agent. They point out that overdosage of irradiated ergosterol may lead to a withdrawal of inorganic salts from the skeleton, especially if the diet is deficient in these constituents. Hypercalcæmia is the outstanding manifestation of the toxic reaction to ergosterol and may be induced by excessive amounts of cod liver oil. Hottinger found that very large amounts of ergosterol when given to puppies produced a reduction in the amounts of both calcium and phosphorus.

"Insulin" and the Amino-Acid Nitrogen Content of the Blood of the Rabbit.

FRITZ BISCHOFF AND M. LOUISA LONG (*Journal of Biological Chemistry*, November, 1929) have made an attempt to establish the conditions under which an "Insulin" hypoglycæmia in the rabbit was accompanied by a definite hypoamino-acidæmia. The experimental procedures are given in detail. Considerable variations were found in the amino-acid nitrogen of the blood in fasting rabbits when a series of readings was taken during twenty-four hours. The values showed a tendency to fall when the animals were made to fast forty-eight hours. Of twenty-five rabbits given subconvulsive doses of "Insulin" only one had a drop in amino-acid nitrogen sufficient to indicate a hypoamino-acidæmia and to obtain this effect it was necessary to keep this animal in a prolonged state of hypoglycæmia by repeated doses of "Insulin." No effect of adrenalin upon the blood amino-acid nitrogen of the rabbit was noted. Premobilization of the glycogen followed by "Insulin" hypoglycæmia was also without action.

Changes of Viscosity in Serum.

ELLA H. FISHBERG (*Journal of Biological Chemistry*, January, 1930) has made an attempt to find the physico-chemical basis of the paradoxical serum viscosities found in certain pathological conditions. The viscosity was measured by the time of outflow through a Poiseuille viscosimeter. Ten cubic centimetres of blood serum were used and the temperature was kept constant. The quotient of the time of outflow of the serum over the time of outflow of pure water through the same viscosimeter at the same temperature was taken as the relative viscosity of the protein solution. Blood serum was found to manifest a remarkable ability to keep its viscosity constant in spite of dilution. This point is regarded as being of great importance in maintaining the circulation of the blood. A protein such as gelatin manifests a great change in viscosity with dilution. The small change of viscosity of the blood serum in nephrosis in spite of the high dilution is due to the special molecular state of the serum proteins. The high viscosity of blood serum in cyanosis was found to be due to the migration of water from the serum into the corpuscles, due to the necessity of maintaining the equilibrium of diffusible ions (Donnan's equilibrium) and the equilibrium of osmolar concentration. It has been known for some years that urea decreases the viscosity of water and it was found that the viscosity of blood serum is similarly decreased by the addition of urea. The decrease found was small but definite and on repeated observations outside the limit of error. In five patients with uræmia all of whom had abnormally high urea figures, the author found that the viscosity was fairly normal, owing in some measure to the depression in the viscosity caused by the higher urea concentration, even though there was a great increase in the amount of total solids in the serum. In obstructive jaundice the bile acids raise the viscosity which is low in pernicious anæmia and hæmolytic jaundice in spite of the high bilirubin content.

British Medical Association News.

SCIENTIFIC.

A MEETING OF THE NEW SOUTH WALES BRANCH OF THE BRITISH MEDICAL ASSOCIATION was held at the Royal Alexandra Hospital for Children, Camperdown, on November 14, 1929. The meeting took the form of a series of clinical demonstrations by members of the honorary staff.

Typhoid Spine.

DR. E. H. M. STEPHEN showed a girl, aged twelve years, who had complained of nausea five days before admission. She had not vomited, but had been listless and feverish on the following day. She had suffered from anorexia. Her stools had been fluid, brown and slimy and she had had four motions a day. She had not suffered from epistaxis. According to the previous history she had suffered from pertussis, mumps, measles and varicella.

On admission she had looked very ill and thin. No pain had been present. The tongue had been red and furred and the tonsils of medium size and slightly injected. The abdomen had appeared very wasted. The spleen had not been palpable. No reaction had been obtained to the von Pirquet test. Subsequently the spleen had become palpable. The leucocytes had numbered 6,400 per cubic millimetre. No growth had been obtained after inoculating a culture tube from the blood. The urine had at first been clear, but subsequently a trace of albumin had been discovered with numerous motile organisms, but no pus cells. *Staphylococcus albus* had been obtained on culture. Later on *Bacillus coli communis* had been grown from the urine. On inoculating a culture tube from the stool lactose fermenters had first been grown and then *Bacillus coli communis*. The blood at a later stage had yielded a response to the Widal reaction. The patient had then complained of pain in the lumbar region. On examining the lumbar vertebræ the radiologist had reported the presence of typhoid spine. The patient had also suffered from chronic bronchitis and from *seborrhœa capitis*. The optic discs and fundi had been normal, no tubercles had been seen. Klebs-Löffler bacilli had been obtained from a throat swabbing. The patient had gradually improved and had been sent to a convalescent home.

Dr. Stephen said that this complication of enteric fever was distinguished by pain in the lumbar and sacral regions, stiffness in the back and pain on movement, sometimes of the radiating type. There was tenderness on pressure. X ray examination might reveal bony change, usually spondylitis or perispondylitis.

Cretinism.

Dr. Stephen's second patient was a girl, aged eight and a half years, a cretin. She was of Australian and Scotch ancestry. There was no cretinism or goitre in the family. The patient was the eldest of three children; the others were quite normal. The child was backward. She was unable to read or write. She was able to run errands with a note. Her bowels were very obstinate and her motions dry, hard and constipated; frequent enemata were necessary. On X ray examination the *sella turcica* was normal. The bony structure of the mandible was normal. Rhachitic changes were present in the knee. They were mainly old. Both patellæ were ill developed. Ossification was much delayed. Examination of the colon revealed an extremely redundant sigmoid, though no definite Hirschsprung's disease was present. The ends of the diaphyses of the bones of the forearm were more irregular than normal, but otherwise no alteration could be seen. The blood calcium content was normal. Treatment had consisted in the administration of 0·015 gramme (a quarter of a grain) of thyreoid extract twice a day. The child had grown 1·25 centimetres (half an inch) in one month. The weight was unaltered.

Enlarged Thymus and Rickets.

Dr. Stephen also showed a girl, aged ten months. The family history contained nothing of importance. The child had been fed on "Lactogen" since it was three months old and a nævus of the scalp had been removed two weeks previously. The child had suffered from inspiratory stridor and suprasternal recession since birth. It sweated frequently. On X ray examination a diagnosis of persistent enlargement of the thymus and of rickets had been made. The child had been in hospital only one week, but some improvement had occurred as the result of the administration of cod liver oil and milk. It was pointed out that the thymus attained its greatest weight at the age of two years. Any weight above fifteen grammes should be considered abnormal. Enlargement of the Peyer's patches and of the solitary follicles of the intestines was a constant accompaniment. Various lymphatic glands might be enlarged.

Cerebral Tumour.

DR. A. W. CAMPBELL showed a boy, aged three years. According to the history a fainting attack three weeks before admission had been followed by vomiting. The child had been restless and irritable for the following week and three similar attacks had then occurred. One week before admission after a fainting attack the left arm and left leg had been paralysed and the child had been unable to sit up or to walk. He had improved a little, but during the last few days had become worse. Speech and the face had been affected as well. The child had complained of headache and had vomited at intervals during the three weeks. Defæcation and micturition were normal. According to the family history one child had suffered from meningitis, but had recovered. The patient was rather thin and intelligent. The pupils were equal and reacted to light. The corneal reflex was absent on the right side. The right knee jerk was present and the left was exaggerated. The plantar reflex on both sides was extensor in type. Kernig's sign was absent. There was no rigidity of the neck. Paresis was present on the right side of the face; the patient held his head to the left. The tongue deviated to the right. The palate was normal. There was paresis of the left arm and the left leg. There was slight increase of tone of the muscles of the left arm and leg and ankle clonus was present on the left side. Speech was thick and indistinct. The gait was incoordinate; the child fell towards the left side; when sitting in bed, he leaned towards the left side. The ear drums and the mastoids were normal. The optic discs had been examined twice and no abnormality had been discovered. The leucocytes numbered 10,700 per cubic millimetre. No reaction had been obtained to the Wassermann test.

Since the patient's admission to hospital the weakness of the trunk and of the left arm and leg had gradually increased. The child could not sit up in bed. The left arm and left leg had become more spastic. Speech was absent. Swallowing was difficult; the child could not protrude the tongue from the mouth. Paralysis of the right side of the face was absent. Sensation was absent on the right side of the face. There was exophthalmos of the right eye. Although the mental condition had deteriorated a few weeks previously, during the seven days before the meeting the child had become much brighter, he ate more and he attempted to move his right hand and was taking notice of his surroundings.

Dr. Campbell's second patient was a boy, aged nine years, whose illness had begun five months previously with vomiting, headache and failing eyesight. He had suffered from diplopia three weeks before admission, he had had attacks of giddiness, was always thirsty and drank water continuously.

On examination he was seen to be very thin; he was intelligent, but he complained continually of thirst. His pupils were widely dilated; the reaction to light was sluggish and there was no reaction to accommodation. The knee jerks were not obtained. Plantar reflex was not elicited. The abdominal reflexes were present. There was paralysis of the sixth nerve on the left side and possibly some paresis on the right side of the face. The alimentary, respiratory and circulatory systems were normal. The daily output of urine was 960 cubic centimetres. Its specific gravity was 1010. No casts were present. On examination of the fundus double papillœdema

was found with swelling, engorged veins and hæmorrhages. Examination of the blood had yielded the following result:

Erythrocytes, per cubic millimetre	4,500,000
Hæmoglobin value	86%
Colour Index	0·9
Leucocytes, per cubic millimetre	13,000
Polymorphonuclear cells	79%
Lymphocytes	17%
Monocytes	3%
Eosinophile cells	1%

No punctate basophilia was present.

The urea concentration test had yielded a normal result and the blood urea nitrogen was 27 milligrammes per 100 cubic centimetres.

Since admission the child had complained of pain in the head, in the back and in the left flank. He had vomited infrequently. He drank a great deal and passed a large quantity of urine.

Bronchiectasis.

DR. H. G. HUMPHRIES showed a girl, aged eleven years, who was suffering from old standing bronchiectasis. The heart had been pulled over to the left side; the apex beat was in the fifth intercostal space 12·5 centimetres (five inches) from the middle line. The left lung had been deficient in expansion and fibrotic. Definite clubbing of the fingers was present. On November 1, 1929, Dr. Humphries had avulsed the left phrenic nerve. As a result of operation the apex beat had ascended into the fourth intercostal space.

DR. M. J. PLOMLEY showed a boy, aged thirteen and a half years, who had been admitted to hospital on November 1, 1929. In his early childhood he had suffered from pertussis and chicken pox. The family history was normal. Two and a half years previously the patient had suffered from pneumonia and since then he had had a cough. The cough had steadily been getting worse. There was copious and foul smelling sputum. As a rule the patient had only one or two fits of coughing in the day. When he lay on his right side, an attack of coughing was caused. The patient could get rid of large quantities of sputum by making himself vomit. The patient was well nourished, but his fingers were clubbed. Bronchial breathing, râles and bronchophony could be heard over the central portion of the posterior aspect of the lower lobe of the right lung. The extent of the bronchiectasis was clearly seen in a skiagram.

Fibrosis of the Lung.

Dr. Plomley's second patient was a girl, aged ten years. There was no history of tuberculosis in her family. At the age of eight months the patient had suffered from so-called pneumonic influenza in the 1919 epidemic. This had led to bronchitis and subsequent bronchiectasis in the left lower lobe. The patient was suffering from fibrosis of this lobe. The chest had fallen in on the left side and the heart was pulled over in that direction. The right side of the heart lay to the left of the sternum. The patient had been in hospital on several occasions during 1922. No tubercle bacilli had ever been found in the sputum which during the last few years had been copious and offensive.

Syphilitic Arthritis and Keratitis.

Dr. Plomley also showed a girl, aged eight and a half years, who had been admitted to hospital on November 2, 1929, and whose family history was unknown. The patient had always been very healthy and had lived in the country. About three weeks before admission a swelling had formed in the left knee. About ten days later the other knee had also become swollen. The knees were slightly painful and they felt tired and weak when the patient walked.

On examination it was seen that a symmetrical swelling of the knees was present. The swelling was due partly to periarticular thickening and partly to fluid extending to the joint cavity. Movement, except in extreme flexion, caused no pain. The swelling was not tender. Physical examination revealed no other abnormality. Seven days after admission, before the institution of antisyphilitic treatment, interstitial keratitis of the right eye had appeared. A reaction had been obtained to both the Wassermann test and the Kahn test.

Achondroplasia.

DR. MARGARET HARPER showed a girl, aged one year and eight months, who was suffering from achondroplasia. The mother had been married twice. She had had six children by her first husband and all were normal. By her second husband she had two children; the elder was the patient and the younger was a normal baby, six months of age. There was no history of abnormality in the family of either the father or the mother and both father and mother were normal. The child had been breast fed for nineteen months. Ever since birth the arms and legs had been short. Sweating of the head occurred. The child was bright mentally. Occasionally she twitched. The child was small and had a large square head with a widely patent fontanelle. Lumbar lordosis was present. The fingers were short and clubbed. The apex beat was palpable in the fourth intercostal space, 2·5 centimetres (one inch) from the middle line. A pulsation was present in the epigastrium. On percussion the cardiac dulness extended 1·25 centimetres (half an inch) to the right of the sternum and 2·5 centimetres to the left. A loud systolic murmur was audible over the sternum; this was conducted to the right and all over the præcordium. Cyanosis was generalized. The liver was enlarged; its edge was palpable, 1·25 centimetres below the right costal margin. The respiratory system and the nervous system were normal. On X ray examination no definite lesion was seen in the skull. The bones of the legs manifested changes typical of achondroplasia.

The Preparation of Special Diets.

A special demonstration was held in the diet kitchen. Special meals were displayed; they had been arranged to suit the diets, such as fat-free, salt-free and diabetic diets, used in the treatment of various diseases. Dr. Harper explained that the physician gave orders in the ward regarding the number of calories required per day and specified the number of grammes of protein, carbohydrate and fat which he wished used in making up these calories. These orders were translated by the sister in charge of the kitchen into meals of varying foodstuffs and due regard was paid to the provision of a suitable amount of salts and vitamins. The infants' foods were made up in the same way of fresh cow's milk, dried milk and other ingredients, as ordered by the physician. The influence on appetites and digestion of pleasantly served meals was not forgotten. The attractive, brightly coloured trays contained meals which should appeal to the most jaded appetite. The sister also instructed the mother or the patient, if he or she were old enough, in the preparation and weighing and measuring of ingredients for similar meals when the child left hospital.

Erythrœdema with Pulmonary Complications.

DR. LINDSAY DEY showed a female baby, aged twelve months, who had been admitted on October 30, 1929. The patient was an only child. The mother's brother had died of pulmonary tuberculosis. Two months before admission the child had suffered from bronchitis. She had been taken to the country to recuperate and had returned to the city on October 17, 1929, with lobar pneumonia affecting the upper lobe on the right side. After four days the pneumonia had terminated by crisis. The child had not got rid of the cough. On admission the child had been miserable and inclined to be irritable. She had had a cough and at the time of the meeting this was still present. On examination it was seen that the child was flabby; definite hypotonus was present. There was an undue amount of hair covering the body. The hands were pinker and larger than usual. Neither photophobia nor desquamation was present. Râles and rhonchi could be heard in all areas of the chest. The radiological appearances suggested bronchiectasis with superimposed tuberculosis at the upper lobe on the right side. There was a leucocytosis of 12,100 cells per cubic millimetre. The differential count was normal. No reaction had been obtained to the von Pirquet test.

Vesical Calculus.

Dr. P. L. Hipsley showed a girl, aged nine years, who had been admitted to hospital on October 25, 1929. According to the previous history she had suffered from measles and pertussis. Two years previously she had been in the Mater Misericordiæ Hospital for a period of five months, suffering from nephritis. She had passed blood in the urine for six days. No abdominal pain or vomiting and no headache had been present. She had passed urine frequently. She had had a similar attack six months previously. The urine had been turbid and alkaline and on being boiled and allowed to stand the urine in the test tube had consisted of one half albumin. It had contained large numbers of renal cells, pus cells, motile organisms and *Bacillus coli communis* in pure culture. On X ray examination a large vesical calculus had been discovered. The kidneys and ureters had been normal. On November 11, 1929, Dr. Hipsley had made a suprapubic incision and had removed the calculus with some difficulty.

Empyema.

Dr. Hipsley's second patient was a boy, aged five years, who had been admitted to hospital on September 30, 1929. The child had previously suffered from pertussis and scarlet fever. He had complained of pain in the back, in the region of the umbilicus and in the right side for one day. He had slight cough for several days and had been feverish. On admission slight dulness had been present at the right base. The temperature had been 39·7° C. (103·5° F.) and one week later the sputum had become very foul smelling, while the fever had abated. On October 9, 1929, the right side of the chest had been aspirated, but gas only had been obtained. The leucocyte count had been 14,000 per cubic millimetre and smears from the aspirated material had contained Gram-positive cocci and Gram-negative bacilli. X ray examination on October 14 had revealed dulness on the right side of the chest, probably due to pneumonic consolidation of the whole of this lung with some fluid along the lateral aspect and at the base. Operation had been performed on October 15, 1929. Pus had been found on exploring the right axilla posteriorly. Portion of a rib had been resected and on excision of the pleura very foul smelling pus had escaped. A tube had been inserted. Culture of the pus had revealed long chain streptococci and what were regarded as influenza bacilli. The wound was draining well. The cough had practically vanished, the temperature was normal and the patient's condition much improved.

Congenital Dislocation of Both Hips.

Dr. Hipsley also showed a girl, aged eighteen months, who had been admitted on March 18, 1929, because the parents had noticed a limp when the child tried to walk. On examination the pelvis had been found to dip on both sides. The trochanters had been prominent and the perineal region wide. X ray examination had revealed double congenital dislocation of the hip. On March 20, 1929, the heads of the femurs had been manipulated into position and the child had been placed on a Hipsley frame. The right hip had proved refractory, but had eventually been got into position. On removal of the splint difficulty had been experienced in bringing the legs down, particularly the right. On October 15, 1929, attempts to bring the leg down under anæsthesia had failed owing to contracture of the muscle. Subcutaneous tenotomies had been performed on the muscles attached to the anterior superior spine of both ilia. The child had been placed on a Jones's abduction splint and extension by means of strapping applied. Dr. Hipsley pointed out that the legs had come down well and that the femoral heads were in good position.

Tuberculosis of the Spine.

Dr. Hipsley also showed a girl, aged seven years, who had been admitted to hospital on March 25, 1926. Hibbs's operation for tuberculosis of the spine had been performed. Five months later a psoas abscess had formed on the right side and had been aspirated. A discharging sinus had formed in the abdominal wall and irrigation had been carried out with Dakin's solution. Later on a counter-opening had been made and eventually the sinus had healed.

Dr. F. C. Rogers showed a boy, aged one year and eight months, who had been noticed to hold his head in a peculiar fashion for two months prior to admission. He had also manifested a peculiarity of gait since his first attempt at walking a few months previously. Inquiry into the family history revealed the fact that an aunt had died of pulmonary tuberculosis twelve months before. The patient's tonsils and adenoids had been removed at the Renwick Hospital for Infants two months before his admission.

On admission the child had been noticed to hold his head tilted in a backward direction and to keep it very steady. On walking he had held his head backwards, the chest had been projected well forward and the body tilted forward from the pelvis. A projection had been present over the upper part of the thoracic portion of the spine. The lumbar curve had been absent. A von Pirquet test had been carried out and a reaction obtained to both human and bovine types of organisms. On radiological examination appearances suggestive of early tuberculosis of the fourth thoracic vertebra had been found. There had also appeared to be great enlargement of the thymic shadow. An area of pronounced dulness had been present in the right interlobar region, regarded as being produced by an area of resolving pneumonia. The patient had been placed in Rollier straps. Two days later he had had some difficulty with his breathing after an attack of coughing, as though there was some obstruction to inspiration. At other times respiration was normal. A week later it had been noted that the patient had slight difficulty in swallowing and that respiration was noisy and prolonged while he was lying quietly. On examination dulness had been discovered at the right apex with tubular breath sounds and increased vocal resonance over the same area. The temperature had been normal and there had been no increase in the respiratory note. It had been decided to apply deep X ray therapy to the thymus gland.

Spina Bifida.

Dr. Shedden Davis showed a girl, aged two weeks, who was suffering from *spina bifida*. The patient was the sixth child; the others were normal. On examination she appeared anæmic and looked ill. A large swelling was present over the upper sacral and lower lumbar areas of the spine. The skin was thin and broken in several places. The swelling which had been five centimetres (two inches) in diameter on admission, had gradually enlarged. It was soft and fluctuant. Movement of the legs was present, though not free. The legs were kept flexed and the feet in a *varus* position. The legs were definitely weak.

Hirschsprung's Disease.

Dr. Shedden Davis also showed a boy, aged four months, who was suffering from Hirschsprung's disease. There was one other child in the family and it was quite well. The child had been normal up to the age of two months. At that time the abdomen had become swollen and constipation had been absolute. Occasional vomiting had occurred. The child was a "Lactogen" baby and took his food well. On admission he had been very wasted and listless. The abdomen had been enormously swollen and the outline of the large bowel had been quite obvious. Peristalsis had been visible. The abdomen had been very tympanic and liver dulness had been increased by the colonic enlargement. Left lumbar ramisection had been performed. Seven days after admission it had been noted that the child alternately gained and lost weight. The abdomen had still been distended, but this had been relieved by enemata of saline solution and of permanganate of potash solution given every day. Occasional passage of the rectal tube afforded relief. The patient was taking "Dimol" four times a day and thyreoid extract 5·4 milligrammes (one-twelfth of a grain) twice a day as well as paraffin and cascara. X ray examination had revealed an enormous dilatation of the colon, the appearance being typical of generalized Hirschsprung's disease.

Talipes Equino-Varus.

Dr. Shedden Davis's last patient was a boy, aged five years, who suffered an extreme degree of bilateral *talipes equino-varus*. The feet had been at right angles to the tibiæ, the toes pointing in a medial direction with the dorsum of the foot on the ground and the plantar surfaces facing in a directly posterior direction. The *calcaneus* on each side pointed upwards. The position of the *talus* in each foot was normal. Hyperkeratosis with an underlying bursa was present on the dorsum of each foot. The patient had been able to stand upright and to walk and run with moderate difficulty, the feet being kept well apart. Operation had been performed on the right foot three days after admission and it had been put on a back splint. Massage had been commenced and strapping applied eleven days after operation. Operation had been performed on the left foot fifteen days after that on the right and the same after treatment had been adopted.

Syphilis.

DR. D. G. R. VICKERY showed a girl, aged nineteen months, who had been brought to the out-patient department by her mother on July 3, 1929, on account of inability to control an umbilical hernia by means of strapping. The strapping had been used for a period of six months. The child had been pale and had shown evidence of malnutrition. She had not been walking and the abdomen had been much eniarged with a protruding umbilical hernia. The fullness had been more pronounced in the upper half of the abdomen. Tortuous veins from the umbilical region had run upwards towards the lower border of the ribs, suggestive of some obstruction to the portal circulation. The liver had been palpable at the level of the umbilicus, its surface had been smooth and its edge hard and sharp. The spleen had been enlarged to about three times its normal size and the notch easily palpable. Both the child and her mother had yielded a "+++" response to the Wassermann test (the patient was an only child and the mother had had no miscarriages). The patient was being treated by mercurial inunction and injections of "Neokharsivan," together with a mixture containing iodide of potash 0·03 gramme (half a grain) three times a day. Dr. Vickery pointed out that the general health of the child had improved to a considerable degree and that the liver was slightly smaller and definitely softer.

The mother had come under treatment ten weeks prior to the birth of another child. This child had been born at full time; it had appeared to be perfectly healthy, but had yielded a reaction to the Wassermann test.

NOMINATIONS AND ELECTIONS.

THE undermentioned have been nominated for election as members of the New South Wales Branch of the British Medical Association:

Wiseman, John Elliott, M.B., B.S., 1929 (Univ. Sydney), Sydney Hospital, Sydney.

Audley, William Ernest, M.B., 1929 (Univ. Sydney), c.o. Dr. Hodgkinson, Orange, New South Wales.

Maffey, Reginald Errol, M.B., B.S., 1929 (Univ. Sydney), c.o. Mrs. Falkiner, Roslyn Avenue, Roseville.

LISTS OF MEMBERS.

THE lists of members of the several Branches of the British Medical Association in Australia are now available. Copies can be purchased from the office of THE MEDICAL JOURNAL OF AUSTRALIA at one shilling each.

Medical Societies.

THE BRISBANE HOSPITAL CLINICAL SOCIETY.

A MEETING OF THE CLINICAL SOCIETY OF THE BRISBANE HOSPITAL was held at the Brisbane Hospital on August 8, 1929, DR. E. S. MEYERS in the chair. The meeting took the form of a series of clinical demonstrations.

Intestinal Obstruction.

DR. ALAN E. LEE showed a young adult male who had presented himself at hospital with a typical history of acute appendicitis of twenty-four hours' duration. On examination the abdomen had been rigid over its lower half with widely diffused tenderness. Under general anæsthesia and through a Battle's incision, a gangrenous perforated pelvic appendix was removed. As much of the free peritoneal exudate as possible had been aspirated and a tube had been placed into the recto-vesical pouch through a suprapubic stab wound. The main incision had been completely closed. The drainage tube had been removed on the third day. The patient's condition had remained good for one week, except that some infection of the main wound had been present. Moderate diarrhœa and gradually increasing abdominal distension had then set in. Repeated rectal examinations had not revealed any pelvic collection of pus. By the seventeenth day after operation the distension had increased to such an extent that it was deemed wise to reopen the abdomen.

At this operation a widespread condition of adhesion formation had been found. The small gut had been enormously distended, the actual source of the obstruction seeming to lie in a massive adhesion of coils of ileum to the bottom of the pelvis. It had appeared unwise to try to release these, so a distended loop of ileum had been perforated, as many coils as possible milked empty and a tube inserted into the opening. Abundant drainage had taken place during the next fourteen days, when further operation had been undertaken.

Under spinal anæsthesia the intraabdominal condition had been again inspected. The number of adhesions present had been so great that it appeared an almost impossible task to expose the obstructed loop in the pelvis. The small intestine had therefore been followed downwards as far as possible from its upper end. A loop had been found which appeared to be the entering loop of the ileostomy. This had been divided, the lower end closed and the upper implanted into the side of the transverse colon. The patient had convalesced normally and five weeks afterwards had reported a gain in weight of 6·3 kilograms (14 pounds).

Dr. Lee, after discussing the nature of intestinal obstructions after appendicectomy, said that he thought this case illustrated two points: First, the wisdom of doing nothing more than an ileostomy in the presence of acute obstruction or in the case of a neurogenic obstruction merely doing a jejunostomy and, secondly, that it was preferable to short-circuit the original obstruction rather than to remove it, if the removal appeared to be a difficult or hazardous task.

Hypernephroma.

DR. J. J. POWER showed a patient in conjunction with Dr. Hedley Brown. A married woman, aged thirty-two years, had been confined on June 16, 1929, by Dr. Brown of the fifth child which weighed 3·3 kilograms (seven and a half pounds). The confinement had been normal. At that time there had been discovered a large tumour in the right kidney area. This had been quite symptomless. On June 30, 1929, the patient had been admitted to hospital and a cystoscopic investigation had been carried out.

Excretion of indigo carmine, injected intravenously, had been normal in time and quantity from the left ureter, but there had been no dye in twenty minutes from the right ureter. The ureteric orifices and the bladder had been normal. A right ureterogram and pyelogram had been prepared and this had shown the right ureter displaced and occupying a position over the centre of the bodies of the lumbar vertebræ. The pelvis of the kidney

had been displaced upwards and distorted and flattened. Two major calices and minor calices had been seen which did not present any abnormality.

The diagnosis seemed to rest between a tumour on the lower pole of the kidney or a perirenal tumour; the distortion as well as displacement of the pelvis had favoured a kidney tumour.

On July 12, 1929, a nephrectomy had been performed; the tumour, examined microscopically, had been diagnosed as a hypernephroma. Convalescence had been uneventful.

Lupus Erythematosus.

Dr. B. B. Barrack showed a patient who was suffering from *lupus erythematosus* and who was under treatment with intravenous injections of gold sodium thiosulphate. She was an unmarried woman, aged sixty years, who had been born and had lived in Ireland. She had come to Australia three years previously. She had suffered from *lupus erythematosus* for nine years and had been treated in Dublin and London with quinine internally, also with light therapy. There was a family history of seven brothers and six sisters having died of tuberculosis. The patient was a well nourished healthy looking woman. Both cheeks, chin, nose and forehead were extensively affected, with a few patches outside these areas. On July 11, 1929, she had been given 0·05 gramme of gold sodium thiosulphate intravenously and a similar amount on July 14, 1929. Up to August 5, 1929, she had received six injections. An improvement had been noticed after the second injection and had been maintained. Dr. Barrack intended giving twelve to fifteen injections; the dose had not been increased owing to the patient reacting to some of the injections. Dr. Barrack said that during the last two years he had treated some six or seven patients with *lupus erythematosus* with injections of gold and all had responded to the treatment; one patient's lesions had flared up after exposure to sunlight for several days and had necessitated a further course.

The family history of tuberculosis was of interest, as *lupus erythematosus* was regarded by some authorities as a toxic disease of tuberculous origin. This was the first of Dr. Barrack's patients who had given any history of interest. He hoped to show her again when she had completed her course of treatment.

Leprosy.

Dr. Barrack also showed a patient who was suffering from nodular (tuberculous) leprosy. The patient, a man, aged sixty-five years, lived in Nambour in the north coast district of Queensland. There was a history of association with a leper fifteen to twenty years before. The clinical manifestations in this patient were most striking, the body and limbs being covered with nodules. The lobes of the ears, the cheeks and forehead were heavily infiltrated. A section of a nodule manifested Hansen's bacillus. Patches of anæsthesia were sought for, but none was found.

Epithelioma of the Lip.

Dr. E. S. Meyers showed a man of fifty years of age who had suffered from an epithelioma of the lip for six months. The lip had been treated by radium puncture and the glands of the submaxillary region had been removed by means of the Liebel Flarseleim electric scalpel. The glands were infected with cancer cells, as was shown by a microphotograph. It was proposed to treat the area of the neck by distance radiation.

Dr. Meyers also showed a patient who had suffered from epithelioma of the uvula and base of the tongue. The glandular areas of the left side of the neck had been removed and had been proved to be infected with cancer cells, cell nests being present in the glands, as was shown by a microphotograph. The glands of the right side of the neck which had also been removed, were likewise infected with secondary deposits. It was proposed to treat the neck with distance radiation.

The question in these two patients was raised as to whether it was better to remove the glandular areas draining an original cancer focus, following this with distance radiation or whether the whole of the glandular areas of the neck should be removed with the subsequent use of distance radiation.

Radium and Cancer of the Tonsil.

Dr. Meyers showed an X ray photograph in connexion with a patient suffering from cancer of the tonsil extending to the vallecula. The X ray picture showed three radium needles *in situ*. The difficulty of keeping needles in position in this situation was emphasized. The method of inserting the needles in the patient in question was as follows. The sterno-mastoid muscle was cut through at its insertion and turned downwards. The posterior belly of the digastric muscle was then cut through and following this the internal jugular vein and glands were removed *en bloc*. The internal carotid artery was then retracted and the three needles were inserted as shown in the skiagram.

Tuberculosis of the Bowel.

The last patient shown by Dr. Meyers was a Solomon Islander, aged seventy years. He had suffered from intestinal obstruction caused by a growth at the ileo-caecal valve and had been shown at a previous clinical meeting in June, 1929. On that occasion the caecum had been delivered on to the abdominal wall and the small bowel drained by a large catheter. Subsequent to this an ileo-colostomy had been performed, the ileum being joined to the transverse colon by a lateral anastomosis. One week before the meeting the growth had been excised and the two ends of the bowel had been closed and a drainage tube inserted at the site of closure. Dr. Taylor had reported that the growth was tuberculous.

Hemiplegia with Illusions.

Dr. John Bostock showed a middle aged woman who in September, 1928, had suffered from a right sided hemiplegia. This had cleared up, but she had returned to hospital some months later with hemiplegia on the opposite side. The Wassermann test had yielded no reaction; her systolic blood pressure was 200 millimetres of mercury. The lesion appeared to be vascular in origin. The fact that the patient could talk rationally about ordinary topics of conversation was readily demonstrated; that none the less there had been grave derangement of her cerebral tissues was shown by the existence of definite illusions. She considered that a little boy was in bed with her and based this conclusion on the evidence that her paralysed left hand and foot belonged to him. She protested that it was absurd to argue her out of the belief and expressed concern that since being in hospital the little fellow had not had any food. She wondered how he was nourished. Dr. Bostock pointed out that the above phenomenon showed a definite illusion rather than an hallucination, since peripheral stimulus was present, but not the one which would cause the particular percept. The patient was interesting as showing the genesis of a definitely psychic abnormality on a physical basis.

Hypothryeoidism.

Dr. N. W. Markwell showed a middle aged *multipara* with hypothyreoidism, but with the original complaint of losing 6·3 kilograms (a stone) in weight in twelve months as well as being very weak for years. She was unusually thin and the pulse rate was rapid. The basal metabolic rate was reported as being −53%. She was more tolerant of thyreoid extract than the usual myxœdematous patient, a daily dose of 0·54 gramme (nine grains) being reached within a month. She was taking 0·42 gramme (seven grains) a day. The diagnosis seemed unequivocal, as she had after three months' treatment regained her strength and she had lost the pronounced yellow appearance of her skin. The skin was clear, whilst a haggard and unattractive facies had been replaced by quite an attractive appearance, making her almost unrecognizable. She had had a diseased ovary removed some years previously, about the time of the onset of the weakness. No other treatment had been given.

Malignant Growth of the Sigmoid.

Dr. Markwell also showed a patient with a new growth in the sigmoid colon complicated by a "++++" response

to the Wassermann test. The main point of interest was that with a barium enema no abnormality had been found, but the growth had been visible through the sigmoidoscope. The patient was an aged man who had had diarrhœa for months with increasing weakness. He had an intermittent temperature until after several arsphenamin injections and his general health had improved at the same time. He could not tolerate bismuth or iodine as iodides or iodone. Nevertheless, a recent sigmoidoscopic examination showed that the growth was almost certainly a malignant one. The surgeon did not think the patient was fit for operation.

Cardiac Syphilis.

Dr. Markwell also showed a middle aged *multipara* who was suffering from syphilitic auricular fibrillation. She had been admitted into one of Dr. Alex Murphy's beds with congestive œdema. A "++++" response had been obtained to the Wassermann test. As well as treatment by digitalis in the orthodox manner combined with "Novasurol" she had been given arsphenamin after a preliminary course of bismuth. After four months in hospital she had been discharged to the out-patient department feeling well, except for shortness of breath on considerable exertion.

She was having a second course of bismuth and arsphenamin; these were being given together after a preliminary course of iodides. The heart's action had become normal with quinidine in hospital and, after return of the fibrillation, spontaneously in the out-patient department. The effects of the antisyphilitic treatment were to be discounted in this connexion as she gave a history of a period of irregular action many years before.

The long waves of *QRS* were blurred. There was no rheumatic history. This patient was shown to draw attention to the possibility of syphilis in any heart condition. At many large American clinics a routine Wassermann test was carried out in every patient with a cardiac lesion. Statistics from the United States of America seemed to show that at least 10% of cardiac patients gave a positive response to the Wassermann test.

Post-Graduate Work.

ANNUAL COURSE IN BRISBANE.

THE Council of the Queensland Branch of the British Medical Association announces that it will hold its annual post-graduate course in Brisbane from June 2 to 6, 1930.

Dr. S. V. Sewell, of Melbourne, will deliever a lecture on medical subjects and will give a demonstration. Dr. Alan Newton, of Melbourne, will deliver a lecture on the surgery of the upper regions of the abdomen and will demonstrate some abdominal operations. Dr. R. Gordon Craig, of Sydney, will deliver the Bancroft Oration on June 6, 1930. The title of the oration will be "Progress in Prostatic Surgery." It will be illustrated by a cinematograph film prepared by the American College of Surgeons on prostatic enlargement. Dr. G. A. C. Douglas, of Brisbane, will give a demonstration on the treatment of fractures of the femur.

The subscription to the course is two guineas. This will include attendance at the lectures and demonstrations and also a double ticket for a dance and bridge party to be held on June 2, 1930.

Members are asked to notify the joint Honorary Secretaries, Dr. Neville G. Sutton and Dr. Keith Ross, British Medical Association Building, 35, Adelaide Street, Brisbane, as early as possible, that they intend to be present and to intimate whether or not they will be accompanied by their wives.

COURSE IN APPLIED PATHOLOGY IN MELBOURNE.

THE MELBOURNE PERMANENT COMMITTEE FOR POST-GRADUATE WORK announces that a special course of ten lecture-demonstrations on recent advances in applied pathology will be given at the University of Melbourne by Professor P. MacCallum in April, May and June, 1930. The lecture-demonstrations will be delivered each Tuesday at half past eight o'clock in the evening. The fee for the course is three guineas. Those who intend to participate are requested to send their names to the joint honorary secretaries, Dr. Harold Dew and Dr. W. S. Johnston, 12, Collins Street, Melbourne, as soon as possible and to remit the amount of the fee. Further particulars will be forwarded on application. The following is a summary of the course. The date of the first lecture has been altered.

Tuesday, April 1, 1930.

The blood and hæmopoietic tissues; the nature and relationships of the reacting tissues; the balance of blood cell formation and destruction; differential cellular responses to pathological conditions disturbing the balance; the stability of the erythrocyte; hæmoglobin and iron metabolism; the plasma and blood volume; the peripheral blood as a pathological index.

Tuesday, April 8, 1930.

The blood and hæmopoietic tissues (continued); the interpretation of specific diseases of the blood; secondary and primary anæmias; *polycythæmia rubra*; the leucocythæmias; the spleen and anæmias; tumour relationships.

Tuesday, April 15, 1930.

Inflammatory and degenerative conditions of the arteries; anatomy; changes with age; the incidence, pathogenesis and ætiology of arteriosclerosis; fatty deposits, atheroma and calcification; hyaline and amyloid degeneration; the arteries in diabetes; productive endarteritis; mesarteritis; *thromboangiitis obliterans*; purulent arteritis; *periarteritis nodosa*; syphilitic arteritis; aneurysms.

Tuesday, May 6, 1930.

Bone; origins and relationships of the tissue; conditions of development and maintenance; calcium and phosphorus; endocrines; vitamins; pathological bone formation and resorption; histology, fractures and repair; non-union; acute osteomyelitis and periostitis.

Tuesday, May 13, 1930.

Bone (continued); chronic osteomyelitis and osteitis; tuberculosis; syphilis; rickets and infantile scurvy; the osteomalacias, *osteitis fibrosa* and *osteitis deformans*; age, endocrines and diet; tumours of bone.

Tuesday, May 20, 1930.

Cardiac pathology; (*a*) the myocardium, the blood supply and arterial disease, atrophy and degeneration, the ætiology and consequences of parenchymatous and interstitial myocarditis, acute and chronic, the conducting system of the heart and pathological lesions; (*b*) endocarditis, ætiology, pathogenesis and bacteriology.

Tuesday, May 27, 1930.

The liver; structure, blood supply and lymphatic connexions in relation to function and the localization of the effects of circulatory disturbances, intoxications and infections; hæmorrhage, degenerations, focal necrosis and suppuration; regenerative power of liver tissue; acute yellow atrophy and the cirrhoses; tumours and tumour dissemination.

Tuesday, June 10, 1930.

The liver (continued); pathological physiology; experimental pathology; carbohydrate, protein, fat and cholesterin metabolism; detoxication of blood; ascites; bile formation.

Tuesday, June 17, 1930.

Diseases of the mammary gland; structure and functional relationships; lactation and involution; acute and chronic mastitis; precancerous changes; the diagnosis of innocent and malignant tumours; Paget's disease; fat necrosis.

Tuesday, June 24, 1930.

The ovary; development, structure and function and relation to pathology; involution; oophoritis, acute and chronic; cysts and tumours, teratomata, follicular, luteal and blood cysts, endometrioma and carcinoma; parovarian inflammatory and other cysts; connective tissue tumours; secondary growths; the complications and surgical importance of these conditions.

Correspondence.

THE ÆTIOLOGY OF RODENT ULCER.

Sir: Owing to the methods used by Dr. Paul in his reply (in your issue of February 15) to my criticism, I find myself forced once more to beg some of your valuable space, in order to prevent misconception of my attitude and the promulgation of doctrine which cannot be supported by solid facts.

I wish to protest strongly against these methods as shown first in Dr. Paul's use of the ancient rhetorical trick of putting into my mouth expressions I never used. I have never stated that "trauma could never play any part in the causation of rodent tumour." I may have expressed my grave doubts as to whether trauma could play the part of an originating cause, but as an aggravating or an accelerating factor I believe it to be operative in some cases. The use of this trick as instanced in Dr. Paul's last letter to you is quite uncalled for and obviously more befits a political than a scientific controversy.

When it is stated that I was the only dissentient from his finding of trauma as the originating cause of the disease as exhibited in his case at congress, the implication is that I was the only one who disagreed with him. It may well have been that I was the only one who voiced his dissent, but Dr. Paul showed such strong resentment at my disagreement that for peace sake others refrained from expressing their opinions. But even allowing for the sake of argument that his statement is correct, I was, if the bull be excused, in better company than he and his supporters in this instance at least, as I think you will admit when I quote at a later stage the names and words of those who hold the same opinion on this question as I then expressed and still hold more strongly than ever.

The same methods are apparent when my examination of the patient is described as one of the "third degree." This examination lasted not more than one minute, during which I pointed out that the patient had a skin which by its unpigmented character was particularly susceptible to the effects of sunlight, and that she actually showed a solar keratosis of the preepitheliomatous type on another part of the face. This important sign had been overlooked by Dr. Paul or at any rate was not thought worthy of being mentioned to the meeting by him. But not much of that minute can have been left for a "third degree" examination on the history of exposure. Surely one well marked physical sign of sunburn is of more value than a denial of exposure by the patient. When a common and admitted cause is indicated by reason of the presence of a solar keratosis, it is obviously illogical and unnecessary to propound the theory that trauma was responsible, a theory which cannot be supported by quotation of any accepted modern authority nor by any experimental evidence which, however, exists for the ultra-violet ionization hypothesis.[1]

Dr. Paul complains of my use of the term "frequent or important cause" as applied to his belief in trauma as a causative agent. But he mentions two cases which he claims to be due to trauma, out of a total of seventy-five. This gives trauma, according to him, the responsibility of 2·6% of the cases, a proportion that appears important, at least to me, in such a common disease as rodent tumour and much too frequent according to modern evidence. It will be shown later that his proportion of two in seventy-five is many times greater than the barest possibility allowed by a great modern authority.

Let us then grapple now the subject of authority. It is, however, a ridiculously easy task in reality. I first wish to draw attention to the fact that Dr. Paul does not quote against me any recent authors except MacLeod and even his edition is ten years old. No mention is made of Jadassohn and Darier, the two brightest stars of the modern dermatological firmament.

First let us deal with the reference from MacLeod (edition 1920): "In most instances no cause can be suggested for it, . . . On the other hand cases are on record where it has followed some slight injury . . . " Note the cautious "followed" not "was caused by."

Now for Radcliffe Crocker. My edition is dated 1905, but as Crocker died about 1910, I think it was the last. At any rate the quotation made by Dr. Paul occurs verbatim in my edition. But note that Crocker says "a certain number date from a local injury." He does not say any more than MacLeod that they "are caused" by the injury.

As to Stelwagon, I have lost my edition of his book, but he could never be held up as an authority. Even he, however, is cautious and as reported by Paul, "the disease has been noted to start at the site of a scratch, cut or other traumatism."

Dubreuilh I cannot refer to, but as the actual words are not quoted, it is fair to conclude that his expressions were no more positive than those of the other three.

The quotations cited are therefore almost entirely useless to support the contention and I am surprised that such cautious statements should be interpreted as authoritative dicta upon the ætiological problem.

In any case, why bring up a 1905 edition (Crocker) or even a 1920 edition (MacLeod)? (Stelwagon's edition was like the rest, not quoted, but was, I think, 1910). Dr. Paul surely realizes that there have been enormous advances since those times and that it is useless to quote, as authoritative today, opinions enunciated so far back. And it is a fair legal burden that if you quote an authority on one point, you have to accept him on all. Dr. Paul knows that neither Crocker nor even MacLeod so much as mention the influence of sunlight as a possible cause of rodent disease. If the doctrine on trauma is to be accepted, their silence on the other point must be accepted too. Are he and his supporters agreeable to this?

It is pertinent to ask why some more modern opinions could not be quoted in support of the traumatic theory. Take Darier, for instance, who has an edition of 1928. In his "*Précis de Dermatologie*" (1909 edition), page 642, he did in fact mention trauma together with bacterial infections and atmospheric conditions ("*et surtout la lumière*") as possible adjuvants in the production of senile and presenile keratosis and skin epithelioma. But in his 1928 edition, in spite of an exhaustive search, I cannot find trauma mentioned as an ætiological agent except as expressed in the following quotation from page 995:

"Beside the precancerous affections mentioned above" (in the discussion of the causation of which he never mentions trauma) "all scars, in particular those of old burns, of *lupus vulgaris*, of old ulcers and fistulas, exceptionally of *lupus erythematosus*, must be cited."[1]

It is to be noted that he makes no mention, no hint even of the possible rôle of single trauma or insignificant injury such as a scratch. And this was after he had gone fully into the production of cancer by tar, paraffin, arsenic, X rays and radio-active substances *et cetera* and its development in senile and presenile keratoses.

That he is aware of the rôle of sunlight is shown by the following taken from page 471 (1928 edition):

"In the case of persons exposed to the inclemencies (*intemperies*) of weather, sailors (*Seemanshaut*), motorists, aviators, coachmen, farmers and mountaineers, there are to be observed on the uncovered parts of the skin changes altogether analogous to those of xeroderma (? *pigmentosum*) and of senile degeneration. . . . . All

[1] G. M. Findlay, "Ultraviolet Light and Skin Cancer," *The Lancet*, November 24, 1928, page 1070.

[1] This quotation and those that follow have been translated by Dr. Molesworth from the French.

authors report the striking resemblance that is offered by a skin affected with chronic radiodermatitis to the appearances produced by xeroderma and presenile dystrophies. The analogy extends to the epitheliomatous complications which are equally frequent."

Of Jadassohn's opinion on the ætiology of rodent expressed in print I cannot at the moment find an example, though I have searched through a number of reprints which I possess, and which relate to his histological work on basal-celled epithelioma. Unfortunately his second volume of Lesser's *"Lehrbuch"* is not yet published, nor is epithelioma of the skin yet reached in the *"Handbuch der Haut und Geschlechts-Krankheiten"* which he is editing, and of which some twenty-six large volumes have already been delivered to me. But from personal association with him so late as 1927, at a time when my hypothesis (that ionization by ultra-violet light was by far the commonest cause of rodent disease) was exhaustively discussed, I can state positively that while he is more than prepared to accept this hypothesis, he never once so much as mentioned trauma as a possible cause. That he would deny the possibility I gravely doubt, but that he would propound trauma as a cause in any calculable proportion of cases of rodent disease I doubt even more gravely.

From personal association I can give a similar assurance that Whitfield's opinion coincides with those of Darier and Jadassohn.

Most important of all, however, is the considered finding expressed by Roussy in the *"Nouveau Traité de Médecine, fascicule* V, *le Cancer,"* (*Masson et Cie*, 1929). Roussy who must be admitted to be one of the world's foremost authorities on cancer, states, on page 51, after reviewing the literature on the subject of trauma as a cause of the disease and especially the work of Bloodgood who found only two instances of sarcoma out of a total of four hundred cases where trauma could possibly be supposed to have been the causative agent: "Epitheliomas, suspected of being of traumatic origin, are, in the opinion of all authors, much more rare than sarcomas, . . . if one is careful to eliminate the cancers of old ulcers and scars which do not come within the scope of our inquiry."

According to Bloodgood (quoted by Roussy[1]) the possible operation of trauma as a cause of sarcoma is 0·5% According to Roussy who accepted Bloodgood's finding with reserve, all authors agree that epitheliomas "suspected" of being of traumatic origin, are much less frequent. Yet Dr. Paul confidently claims this agency as a cause in 2·6%, *id est* five times as frequently as Bloodgood suspects trauma as operating in the production of sarcoma. How many times more frequent than all authors suspect epithelioma to be due to trauma must be left to the imagination.

On page 52 of the same publication Roussy says that he has never seen a single case resulting from traumatism (his experience being vast and including a multitude of war injuries) and that inquiries made of colleagues of the *Centres Anti-cancereux de France* have only confirmed his views.

On the same page he says: "One must not forget to consider the innumerable cancers of the skin and mucous membranes which appear in the absence of all traumatism. These negative facts, too often left unmentioned, are arguments of great force against the fragile traumatic theory of cancer causation."

But what is the use of bandying authority on this subject, the ætiology of carcinoma being in the melting pot of today from which, however, the dross of traumatic causation has been almost entirely skimmed. It is quite useless to quote ten year old opinions on the cause of epithelioma, even if they were positive (which they are not). But when it comes to Crocker's twenty-five year old book, one might almost as well quote Aristotle or Burton's "Anatomy of Melancholy" for all the value it has as a support for a "fragile" theory of traumatic causation of rodent disease.

[1] Roussy gives the reference as "Prevention, Diagnosis and Treatment of Cancer in its Earliest Stages," by J. C. Bloodgood, *Southern Medical Journal*, Volume XIX, 1926, page 287.

We next come to alternative explanations put forward by Dr. Paul. All are not rodents that are basal celled and Brooke's benign cystic epithelioma, *adenoma sebaceum et cetera*, are not rodents, though the former is a basal-celled growth. It is entirely unimportant for the purposes of this discussion to what cause Dr. Paul wishes to ascribe them.

Nor do unpigmented or pigmented moles develope into basal-celled carcinoma. Darier, with an immense clinical and pathological experience, will only allow them the possible course of development into nævo-carcinoma, *id est* melanoma. (Darier, 1928, pages 959, 992). The same authority (page 264) also lays it down that the lesion best known as seborrhœic or senile wart (as distinguished from the senile keratosis) never developes into epithelioma. Whitfield holds the same view, at least he says he has never seen the occurrence of such a phenomenon.

So all these issues raised by Dr. Paul may be passed as irrelevant.

There remains the question of Cohnheim's theory of "Rests." Really my colleague should breathe an atmosphere of more modern pathology, when he would realize that Cohnheim's theory of "rests" if not discredited, is now held to be incapable of explaining more than a negligible proportion of carcinomatous developments with the possible exception of melanomata and such-like tumours. Let me quote Darier again (1928 edition, page 990). He says, *à propos* of the development of skin carcinoma: "The embryonic inclusions of Cohnheim (and other cognate theories) cannot be reconciled with a very great number of facts."

Some of the facts with which it cannot be reconciled are that rodent occurs more frequently in men than women, in fair than dark people, in whites than blacks, in Australia than in Europe, in outdoor workers than in indoor workers, because no distortion of Cohnheim's theory can explain why "rests" should be more frequent in any one category than another.

Cohnheim's theory, then, will not work as a possible explanation of the occurrence of a rodent growth when subjected to the acid test of facts as stated above.

That basal-celled epithelioma can arise as a result of other causes, unknown, I have always been very careful to stress. They do, though comparatively very rarely, appear in people who have been very little exposed to sunlight and who show no signs of chronic sunburn. But in these very cases there is hardly ever a history of trauma. For all we can tell, they, like Topsy, "just growed." Such exceptional cases can be provisionally explained by Cohnheim's theory if that pleases Dr. Paul, but he must be careful to regard the explanation as provisional and incapable of proof, at present at any rate, as it has been since the enunciation of the theory.

But when one comes to consider the serious contention that a minor trauma such as the scratch of a pin, can induce a basal-celled carcinoma, one must be careful to keep one's sense of proportion.

First, one must remember that patients love to ascribe their cancer to a trauma, for example in breast cases. Yet Sampson Handley[1] could find only one out of his series where he was able to admit the possibility of the correctness of the supposition. And one must not forget the possibility of coincidence in this case. It is the same with other forms of cancer as related by Moran (*The Journal of the Cancer Research Committee of the University of Sydney*, Volume I, No. 1, May, 1929). It is only human nature that the patient must provide an explanation of the causation of his malady satisfactory to his own mind and in rodent disease the claim of the patient that the condition was the result of a minor injury is frequently advanced and is satisfactory to his mind. But would Dr. Paul seriously consider a patient's claim that he contracted malaria by inhaling a miasma, hæmorrhoids by sitting on a cold stone or gonorrhœa from a lavatory seat? Yet these reasons are also frequently advanced by patients as satisfactory.

[1] W. Sampson Handley, "Cancer of the Breast," 1922.

Now let us look at it from another point of view. Trauma of a minor variety is so exceptionally common that, if it had anything like a calculable chance of creating an epitheliomatous development, all of us would inevitably suffer from the disease before we reached fifty years of age. For curiosity I counted and noted the various minor injuries I suffered in a week. Twice I just brought blood with my razor, once I scratched my hand slightly with an uncovered button on a car cushion, on another occasion I just punctured the skin of my face with a twig while looking for a lost golf ball and I slightly jammed a finger in a part of my X ray gear. This may seem a large number, but the week was not specially selected. Busy people are accustomed to such things and our memories fail to record most of them. But five a week is not an overstatement of the average number of small accidents occurring weekly throughout the life of the average man. In childhood these injuries are more common with cuts and scratches, bruises and grazes. And in the case of a manual labourer, a farmer, a gardener, a tradesman, they are considerably more frequent. It is probable, then, that five a week is a reasonable estimate of the average number of such injuries in the average man. Now five minor traumata in a week mean 260 in a year and 13,000 in fifty years.

Let us suppose, then, that five minor traumatic effects occur to each person each week. Let us suppose further that one person in thirty developes rodent if he survives fifty years. This is obviously a very high estimate, but it will operate so as to counteract the possible though not probable error in the first supposition. Now, even if every rodent that occurs be ascribed to trauma, it follows that the chance of a scratch producing a rodent is only one in 390,000. But Dr. Paul himself admits that the proportion of rodents caused by trauma is neither great nor important. Let us therefore reckon them at 1% of the total rodents (Roussy says much less than 0·5%). This reduces the chance to 1 : 39,000,000.

That coincidence must come into operation is obvious and under the conditions of frequently recurring minor trauma it is almost always possible for a patient to remember or imagine a small injury at or about the site of development of the rodent.

Such odds as forty million to one cannot be taken into serious consideration in human affairs and in the ætiology of disease for the reason that the arm of coincidence is far too long.

Therefore, having regard to the safeguarding of our sense of proportion and in consideration of the law of probabilities, we must place trauma, especially of the pin scratch variety, as a highly improbable cause not worth reckoning in the ætiology of rodent disease.

Imagine an Indian walking barefoot all his life, with more than half his body bare, exposed to ten times as much trauma, therefore, as is the case with the European, though protected by his colour from the deleterious influence of too much sunlight. One is forced to expect (if trauma plays even a part in 2·6% of rodent cases in Europeans as Dr. Paul suggests) at least an appreciable number of cases in the teeming millions of India. But according to Muir, except at a development on burns, ulcers and old scars and then as the squamous type, epithelioma of the skin can hardly be said to exist at all in these people.

Dr. Paul says there are none so blind as those who will not see. I agree with him and therefore consider that I must refrain from taking any further part in this controversy until or unless theories advanced are tested by at least a reasonable proportion of the facts or unless a satisfactory hypothesis is advanced to explain the very unequal incidence of rodent disease in whites and blacks, outdoor and indoor workers *et cetera*. At least I feel that I cannot again ask you for valuable space.

Yours, etc.,

E. H. Molesworth.

"Beanbah,"
235, Macquarie Street,
Sydney.
February 24, 1930.

Sir: I recall having read recently in The Medical Journal of Australia a statement to the effect that epithelioma and rodents are not caused by injury. In my twenty-nine years of practice my experience has been to the contrary. To illustrate I will give the history of one case:

In 1904 I was asked by my brother in Ireland to see one of his tenants. Three weeks previously the patient had been injured on the upper lip by the horn of a goat. I advised him to consult his local medical man as I was about to sail for New Zealand. On leaving the country I forgot all about the case and it was not recalled to my mind until I returned to Ireland four years later. Then my brother asked me if I remembered the case and told me that the patient had not taken my advice about seeing a doctor and was then dying of epithelioma of the upper lip. I saw him a few days later when he was beyond surgical aid.

I think one is not justified in excluding injury as an ætiological factor of cancer even of the skin.

Yours, etc.,

J. M. Sterling Levis, F.R.C.S.I.

195, Macquarie Street,
Sydney.
February 24, 1930.

THE MANSON MEMORIAL FUND.

Sir: I was very pleased to read the article headed "Patrick Manson" in the issue of our medical journal of the first instant and to learn that it is proposed to perpetuate the name of this great man by calling the premises to be erected for the accommodation of the Royal Society of Tropical Medicine, "Manson House."

During a holiday in Great Britain in 1899 I had the pleasure and advantage of attending Sir Patrick Manson's course of lectures on "Tropical Diseases" at Saint George's Hospital, London, and of going to and fro with him by train to the "Seaman's Hospital" at the London Docks, and of examining patients from foreign parts, who were under his care in that institution. He gave me the pleasure also at his house of examining microscopically the slides and preparations from which he had demonstrated the developing filariæ of malaria *et cetera* in the thoracic muscles of the mosquito.

He also took me with him to the Charing Cross Hospital and showed me in one of his general wards a patient under his care who had come from India and had the distinct evidences of maculo-anæsthetic leprosy, exactly corresponding with those found by me a short time before in a Chinese patient in South Australia, and so established my diagnosis.

With pleasure I forward you herewith a donation towards the erection of the proposed building which will be a permanent honour to one who has been an ornament to our profession and a benefactor to our race.[1]

Yours, etc.,

Jos. C. Verco.

212, North Terrace, Adelaide.
March 3, 1930.

Naval, Military and Air Force.

APPOINTMENTS.

The undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Numbers 115, 118, of December 12 and 19, 1929, and Numbers 4, 9, 15 and 17, of January 16, February 13, 20 and 27, 1930.

[1] Sir Joseph Verco's donation is £25.—Editor.

PERMANENT NAVAL FORCES OF THE COMMONWEALTH (SEA-GOING FORCES).

Emergency List.

Appointment.—Surgeon Captain Charles Arthur Gayer Phipps (R.N. Retired List) is appointed Surgeon Captain, with seniority in rank of 29th November, 1927.

AUSTRALIAN MILITARY FORCES.

First Military District.

Australian Army Medical Corps.

To be Captain (provisionally)—Thomas Mervyn Seyde Hall, 25th October, 1929.

Major C. J. Weedon, V.D., and Captain H. W. Anderson are transferred to the Australian Army Medical Corps Reserve, 9th December, 1929, and 7th December, 1929, respectively. The provisional appointment of Captain F. G. Scoles is terminated, 31st December, 1929. *To be Captain (provisionally)*—Frank Garrett Scoles, 1st January, 1930.

Honorary Captain J. H. Blackburn is appointed from the Australian Army Medical Corps Reserve and to be Captain (provisionally), 22nd January, 1930.

To be Captain (provisionally) supernumerary to the establishment pending absorption)—Basil Frederick Roberts Stafford, 11th February, 1930.

Second Military District.

First Division: Staff.

Lieutenant-Colonel W. L. Kirkwood, O.B.E., Australian Army Medical Corps, is appointed Assistant Director of Medical Services and is granted the temporary rank of Colonel whilst holding such appointment, 1st January, 1930, *vice* Colonel A. H. Tebbutt, D.S.O., V.D., who relinquishes the appointment on 31st December, 1929.

Australian Army Medical Corps.

To be Captain (provisionally) supernumerary to the establishment pending absorption—Howard Morris Saxby, 18th November, 1929. *To be Lieutenant (provisionally) supernumerary to the establishment pending absorption*—Gilbert Edward Phillips, 18th November, 1929; Captain K. C. T. Rawle is seconded, 1st December, 1929.

Lieutenant-Colonel W. L. Kirkwood, O.B.E., is transferred from the Unattached List with regimental seniority next after Lieutenant-Colonel (Temporary Colonel) R. A. P. Waugh, V.D., 1st January, 1930; Major C. L. Chapman, D.S.O., is appointed to command the 5th Field Ambulance, 1st November, 1929; Captain (provisionally) A. R. H. Duggan and Captain N. H. Meacle are brought on the authorized establishment, 1st January, 1930; Colonel A. H. Tebbutt, D.S.O., V.D., is transferred to the Unattached List, 1st January, 1930; the provisional appointments of Captains G. F. Lumley, R. S. Jones and F. G. Roberts are terminated, 31st December, 1929, and they are transferred to the Australian Army Medical Corps Reserve, and to be Honorary Captains, 1st January, 1930.

To be Captains (provisionally) supernumerary to the establishment pending absorption—Solomon Julius and Ivor Gwynne Thomas, 28th November, 1929. *To be Lieutenant (provisionally) supernumerary to the establishment pending absorption*—Harley Irwin Turnbull, 13th December, 1929. Captain (provisionally) A. W. Morrow is brought on the authorized establishment, 1st November, 1929.

To be Lieutenant (provisionally) supernumerary to the establishment pending absorption—Andrew Arthur Abbie, 13th January, 1930.

The provisional appointment of Captain G. Cummins is terminated, 4th January, 1930. *To be Captain (provisionally)*—Lieutenant G. Cummins, from the Reserve of Officers, 5th January, 1930.

Major C. L. S. Macintosh, D.S.O., is transferred from the Unattached List with regimental seniority next after Major W. Vickers, D.S.O., and is supernumerary to the establishment pending absorption, 1st October, 1929; the provisional appointments of Captains H. J. Foley and W. E. Audley are confirmed.

Australian Army Medical Corps Reserve.

The resignation of Lieutenant-Colonel H. R. G. Poate of his commission is accepted on his appointment to a commission in the Royal Australian Air Force; Honorary Captain L. C. Webster is retired, 3rd December, 1929.

Majors E. B. G. Riley and C. Cosgrove, M.C., Captains W. G. Robinson and H. V. Gillies and Honorary Captain H. Z. Throsby are retired.

Honorary Captain J. Pirie is retired, 24th January, 1930.

Third Military District.

Australian Army Medical Corps.

Lieutenant L. Smith is transferred (provisionally) from the Melbourne University Rifles, 4th Division, and is supernumerary to the establishment pending absorption, 30th August, 1929; the provisional transfer from the 32nd Battalion, 4th Division, of Lieutenant E. J. Grieve, is confirmed.

To be Colonel—Lieutenant-Colonel (Temporary Colonel) J. A. H. Sherwin, V.D., 1st December, 1929.

The provisional appointment of Lieutenant L. E. Odlum is confirmed. Captain A. J. G. Mackay ceased to be seconded, 10th December, 1929.

The resignation of Lieutenant H. M. Hill of his provisional appointment is accepted, 9th January, 1930.

Captain A. J. G. Mackay is brought on the authorized establishment, 11th December, 1929; the provisional appointment of Captain R. W. S. Fox is terminated, 31st December, 1929, and he is transferred to the Australian Army Medical Corps Reserve, 1st Military District, and to be Honorary Captain, 1st January, 1930.

To be Captain (provisionally) supernumerary to the establishment pending absorption—John Strahan Bothroyd, 6th February, 1930.

Australian Army Medical Corps Reserve.

Major W. B. Craig, D.S.O., is placed upon the Retired List with permission to retain his rank and wear the prescribed uniform, 24th November, 1929; Captain J. L. Thompson is retired, 13th December, 1929.

Honorary Captain G. W. Foster is retired, 11th January, 1930.

Fourth Military District.

Australian Army Medical Corps.

Lieutenant B. S. Hanson is transferred (provisionally) from the Australian Field Artillery and to be supernumerary to the establishment pending absorption, 21st January, 1930.

Australian Army Medical Corps Reserve.

The resignation of Captain (Honorary Major) E. A. Johnson, V.D., of his commission is accepted, 17th January, 1930.

University Intelligence.

THE UNIVERSITY OF SYDNEY.

A MEETING of the Senate of the University of Sydney was held on March 3, 1930.

It was resolved to inform the Director-General of Health for the Commonwealth that the Senate offered no objection to the proposal to inaugurate as portion of the activities of the School of Public Health a medical service and supervision of undergraduates on the understanding that it did not imply compulsion in that direction.

Dr. Arthur Webb, Dr. A. J. Traill, Dr. J. Godsall and Dr. J. L. Harrison were appointed Honorary Demonstrators in the Department of Anatomy for the year 1930.

The following appointment was confirmed:

Dr. Francis Lions as Acting Professor of Organic Chemistry during the absence on leave of Professor J. C. Earl.

Books Received.

HANDBOOK OF BACTERIOLOGY FOR NURSES, by Harry W. Carey, A.B., M.D.; Third Revised and Enlarged Edition; 1930. Philadelphia: F. A. Davis Company. Demy 8vo., pp. 282, with illustrations. Price: $2.25 net.

THE IMPROVED PROPHYLACTIC METHOD IN THE TREATMENT OF ECLAMPSIA, by Professor W. Stroganoff; Third Edition, thoroughly Revised and Completed; First English Edition; 1930. Edinburgh: E. and S. Livingstone. Crown 8vo., pp. 160. Price: 10s. 6d. net.

THE LIFE OF HERMANN M. BIGGS, M.D., D.Sc., LL.D.; PHYSICIAN AND STATESMAN OF THE PUBLIC HEALTH, by C. E. A. Winslow, Dr.P.H.; 1929. Philadelphia: Lea and Febiger. Royal 8vo., pp. 432, with illustrations. Price: $5.00 net.

THE FUNDAMENTALS OF BACTERIOLOGY, by Charles Bradfield Morrey, B.A., M.D.; Fourth Edition, thoroughly revised; 1929. Philadelphia: Lea and Febiger. Post 8vo., pp. 347, with illustrations. Price: $3.50 net.

ANNALS OF ROENTGENOLOGY: A SERIES OF MONOGRAPHIC ATLASES, Edited by James T. Case, M.D.; Volume IX: The Neck, by Percy D. Hay, Jr., M.D., with an Introduction by Henry K. Pancoast, M.D.; 1930. New York: Paul B. Hoeber, Incorporated. Demy 4to., pp. 124. Price: $8.00 net.

OTOLOGIC SURGERY, by Samuel J. Kopetzky, M.D., F.A.C.S.; Second Edition, Revised; 1929. New York: Paul B. Hoeber, Incorporated. Royal 8vo., pp. 570, with illustrations. Price: $8.00 net.

A MANUAL OF PROCTOLOGY, by T. Chittenden Hill, Ph.B., M.D., F.A.C.S.; Third Edition, thoroughly revised; 1929. Philadelphia: Lea and Febiger. Post 8vo., pp. 272, with illustrations. Price: $3.50 net.

MECHANO-THERAPY: A TEXT-BOOK FOR STUDENTS, by Mary Rees Mulliner, M.D.; 1929. Philadelphia: Lea and Febiger. Post 8vo., pp. 265, with illustrations. Price: $2.75 net.

Diary for the Month.

MAR. 18.—New South Wales Branch, B.M.A.: Medical Politics Committee.
MAR. 19.—Section of Obstetrics and Gynæcology, New South Wales Branch, B.M.A.
MAR. 19.—Eye, Ear, Nose and Throat Section, Queensland Branch, B.M.A.
MAR. 20.—New South Wales Branch, B.M.A.: Branch (annual).
MAR. 25.—New South Wales Branch, B.M.A.: Council.
MAR. 26.—Victorian Branch, B.M.A.: Council.
MAR. 27.—South Australian Branch, B.M.A.: Branch.
MAR. 28.—Federal Committee of B.M.A. in Australia.
MAR. 28.—Queensland Branch, B.M.A.: Council.

Medical Appointments.

Dr. William Bruce Kirkland (B.M.A.) has been appointed Chief Health Officer for Central Australia.

* * *

Dr. Linda Victoria Magee (B.M.A.) has been appointed Medical Officer, Department of Public Instruction, New South Wales, on probation for six months.

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Dr. Henry Pritchard Elliot (B.M.A.) has been appointed Government Medical Officer at Cooktown, Queensland.

Medical Appointments Vacant, etc.

FOR announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser," page xvi.

BALMAIN AND DISTRICT HOSPITAL, SYDNEY, NEW SOUTH WALES: Junior Resident Medical Officer.

ROYAL NORTH SHORE HOSPITAL OF SYDNEY: Junior Resident Medical Officers.

THE UNIVERSITY OF MELBOURNE: Lectureship in Public Health.

Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCH.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 21, Elizabeth Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company, Limited. Phœnix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane.	Members accepting apopintments as medical officers of country hospitals in Queensland are advised to submit a copy of their agreement to the Council before signing. Brisbane United Friendly Society Institute. Mount Isa Hospital.
SOUTH AUSTRALIAN: Secretary, 207, North Terrace, Adelaide.	All Lodge Appointments in South Australia. All Contract Practice Appointments in South Australia. Booleroo Centre Medical Club.
WESTERN AUSTRALIAN: Honorary Secretary, 65, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.
NEW ZEALAND (Wellington Division): Honorary Secretary, Wellington.	Friendly Society Lodges, Wellington, New Zealand.

Medical practitioners are requested not to apply for appointments to positions at the Hobart General Hospital, Tasmania, without first having communicated with the Editor of THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to "The Editor," THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

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